CLINICAL DIAGNOSIS

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Part One

Regional Diagnosis

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DESCRIPTIVE TERMS

Diagnosis is the art and the science of recognizing the presence or the absence of disease from signs, symptoms or laboratory data, of determining its character and assigning a name thereto. The assignment of the name to a disease often but not always connotes knowledge of the causal factors of the disease; that its character has been determined with reference to type and severity; an estimation of the amount and kind of damage, both general and local, which the patient has received; forecast of the probable course and duration of the morbid process; and cognizance of the personal characteristics of the patient, whether psychic or physical, inherited or acquired.

Purpose of Descriptive Terms. In both the art and the science of diagnosis there are certain descriptive terms of accepted usage, some of historic interest, and others of practical value and convenience, which are used to qualify *diagnosis* and *symptoms* respectively, as now will be shown.

Diagnostic Terms *Anatomic:* based on definite anatomic alterations on which the phenomena depend, a postmortem diagnosis.

Clinical based on the symptoms manifested during life

By Exclusion reached by a deductive process, all the affections which present salient points of similarity with the one to be diagnosed being reviewed in turn, and each successively discarded as one or more of its essential features are missed in a given case, until but one possibility remains, which is accepted as the true one.

Differential the process of distinguishing between different diseases which resemble one another.

Direct: the symptoms are of such a nature that they point to the presence of one special disease and are not capable of misinterpretation.

Pathologic of the nature of a lesion, without regard to its situation. Biopsy: in pathologic diagnosis, usage has established that microscopic examination of living tissue has largely superseded anatomic or postmortem diagnosis.

Physical. by means of physical (objective) signs, irrespective of subjective symptoms, as, for example, by palpation and auscultation.

Presumptive. not regarded as certain.

Retrospective of some antecedent disease or injury, the nature of which can be deduced only from the history given and from the persistent effects

Symptomatic. consisting simply in the determination of the most striking symptoms

Topographic: of the seat of a lesion.

Symptomatic Terms. *Constitutional or General* those that may result from unbalancing of the body as a whole, and are common to diseases of many kinds, especially the severe infections, allergies, and the endocrine and metabolic disorders

Direct those depending directly on the disease.

Local. those which result from localized disease and are usually confined to the site of the diseased organ or tissue

Pathognomonic. those which undeniably indicate the existence of a certain disease.

Reflex those which are caused by local disease, but manifest themselves by means of the nervous system in an otherwise unrelated organ or part of the body

Sympathetic those which appear with the essential ones, but for the presence of which no cause can be assigned except that of sympathy

The Normal (Normal Limits). The term normal as applied to the human b involves an easy assumption of accuracy often entirely unjustified by the facts. well to be cognizant that the use of this term implies a whole series of are known but not expressed For instance, if the expression normal in in reference to an individual, it means that the expositor is aware of the fac many persons differ even from an average mean size of their own race, and fr the members of their own families, and still are within a range of normal size

The anatomic range of the size and shape of the body as a whole is well del ated for each race. Within each race men, women and children can be separa into groups having certain somatic conformations When an individual is found a race who cannot be placed within one of these somatic groups, that individua abnormal for that particular race However, if adjudged by the standards of anotl race, this abnormal individual could become an individual with normal standa for body type For example, a white man or a Negro the size of a normal pyg would, in the United States, be considered abnormal—a dwarf, whereas if amo pygmies, he would be of normal size

Variation in the human body is inherent in all races A good example is afford by the measurements of the female pelvis. One of every 9 white women examin has a generally contracted pelvis. Application of these same measurements to Neg women reveals that 1 of every 3 has a generally contracted pelvis Obstetric expe ence teaches that the generally smaller, contracted pelves, according to the measur ments for white women, may be normal for Negro women The smaller and soft heads of Negro babies pass through these smaller pelves without difficulty

The physician of experience realizes that in order to express a normal or health or qualitative arrangement it is necessary to recognize the average which applies i most instances and the factors which may cause variations from the average. H knows that these factors may cause variations above and below average in particula instances which must still be considered the usual

Two persons of the same race, age and sex may be of the same height, withi the limits of normal as prescribed by height-weight standards, but may have differen body weights. The body weight of one may exceed the specified normal, and the body weight of the other may be less than the normal An experienced physician will appraise the overweight person If the weight exceeds the accepted normal because of excessive body musculature, the individual is accepted as being normal; if the body weight is due to excessive fat, he or she is warned of the excessive weight. The physician likewise will appraise the body weight of the underweight person, if he is convinced that the underweight person eats and sleeps well and suffers no unusual fatigue, he will accept this individual as being within the limits of normal However, if he finds that the underweight person suffers easy fatigue, sleeps poorly and does not eat well, he will attempt to elucidate the reasons for such behavior and will make appropriate recommendations for a betterment of the patient's health

The person who is underweight for the height is often of a particular somatic type, the visceroptotic Many persons of this type are tall and have but little subcutaneous and abdominal fat, so that the skin of the body and abdominal organs sag Formerly persons of this type were considered abnormal The sagging abdominal viscera were upheld by expensive abdominal supports or were subjected to extensive surgical operations to correct the splanchnoptosis Since the visceroptotic type falls within the limits of the normal, neither of these therapeutic procedures benefited the patients. The patients may be returned to health by some gain in weight

Organs and structures have a range of normal variation in size, shape and position. Throughout this text certain measurements for size, shape and position for organs will be given. It is realized that these descriptions merely approach accuracy However, it is better to have an idea of what approaches the normal limits of the size, shape and position of an organ than no idea at all

The range of variation in size, shape and position of an organ depends on many factors, but often on the size and shape of the body as a whole or on aberrations in development and in the range of natural variation. The aberrations in development usually follow certain patterns which can be deduced by a review of the developmental history during intra-uterine life or can be deduced from the history of particular diseases or trauma.

Where bodily function is concerned, a sharp differentiation between inborn variations of health and induced variations of disease or a demarcation between normal and abnormal is not immediately possible. A structure or function showing an extreme degree of variation from the mean may contribute to certain predispositions to disease or injury. The tall man is more likely than the short man to hurt his head when passing through a doorway. Someone who has hyperchlorhydria and a rapidly emptying stomach is more likely under stress and strain to contract or retain a duodenal ulcer than someone who has a less active organ and low gastric acidity. A man who has had a slight stenosis at the neck of the bladder all of his life may begin to have symptoms of prostatism when the prostate becomes insignificantly enlarged at the age of 40 or 45 years. A girl who has had pyelitis during childhood may cease to have any symptoms referable to the urinary tract until her honeymoon or until her first pregnancy. The normals and abnormals in those who have inborn variations of health and induced variations from disease may become differentiable after disease has become established.

The chief difficulties in clinical interpretations are encountered at the extreme ranges of natural variation Variability of one individual from another and variability influenced by age, sex and activity in a species are essential to survival. However, a complete standardization of structure and function would be incompatible with survival. These are statements which refer to the extremes In clinical diagnosis the concern is with the deviations from the usual structure and functions which are indicative of disease. For instance, it cannot be said at exactly what point the pulse ... t what point the heart sounds, the breath sounds, the ... the knee jerk or the ankle jerk, the size and charac- ... ate of the thyroid pass from normality to the stage of disease.

The pulse rate, the blood pressure, the body temperature, the total and differential leukocyte counts, the erythrocyte counts, the concentrations of glucose and urea in the blood, and the basal metabolism are examples of normal range. Single determinations of these phenomena which have a normal range may not be significant in ... n what place ... disease. For ... ml. of blood may lose through hemorrhage a considerable amount of blood, and still the hemoglobin concentration remains within the range of normal. It is the trend of these values established by repeated determinations that is significant in the diagnosis of the normal state or the state of disease. Consequently, the dictionary definition of normal is not the same as when the term is employed by physicians in reference to the human body.

The range of human physiologic and psychologic normality has always been difficult to determine In many physiologic functions statistical methods have been employed. For instance, Ivy says that "a function of the body is statistically normal or usual when its value falls within the central 68 26 per cent of the values found in the same species, race, age and sex " The 68 per cent value is chosen because persons with high and low values of function and without the symptoms of disease are regarded with suspicion. They should not be called abnormal, however, unless other functions and margins of safety can actually be shown to be interfered with or reduced.

and growth are easily confused The growth of a single person may be physiolo normal, though statistically abnormal Slow or rapid growth revealed by the tical method may be suspected of being physiologically abnormal but cannot be sidered abnormal until a cause is found The same is true with aging

Throughout this text attempts will be made, within bounds, to define the n anatomic or physical limits of many important structures The source of such mation has been my own experience and standard textbooks on anatomy but cipally Davis' *Applied Anatomy* and the American edition of Gray's *Anatomy*.

In some instances the physiologic limits of normal will be given. However physiologic limits of normality are often difficult to ascertain, and when data given on physiologic limits of normality these data have been obtained from s of animals not closely akin to man Likewise when there are known definite pa logic changes characteristic of a disease, the gross changes will be stated. More ra will microscopic characteristics be emphasized and then for special reasons.

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THE COMPLAINT AND THE HISTORY

THE COMPLAINT

The term complaint may be used in one meaning only; or it may be employed another meaning only. Often the term is used in different senses at different times without definition. The term admissibly means one of the following: (1) the description of the difficulties which the patient relates to the physician, (2) the symptom or symptoms which cause the patient to visit the physician, (3) the disease or diseases which underlie the symptom or symptoms which cause the patient to visit the physician. Most properly the term seems to mean the first of the three, and so shall it be used in the following discussion

In the clinical record, in order better to elaborate the history, an attempt is made to enumerate the complaints as they are given Some patients will complain of 5 or 10 or more disabilities. Actually, at times, all of these complaints will refer to only one disease. It is usual for the patient who has a functional disorder to make multiple complaints An enumeration of complaints is often diagnostically valuable because such an enumeration will permit of the detection of a disease if present, and also of the functional overlay of symptoms which may be present

The complaint is expressed chiefly by spoken words. Often the words are emphasized by signs, symbols, acts or motions, and under the stress of emotions and pain or profound psychic tension all may not make sense, frequently, therefore, the physician finds himself separated from the complainer because of inability to understand what the complainer means.

In social or business intercourse the formal and polished language of the educated person is a most desirable asset. In the expression of a clinical complaint, however, misplaced elegant words, fine but vague terms, can be at times as disastrous as meaningless words and physical acts. In eliciting the complaint, one should lead the patient to use words that he understands It is the physician's task to understand the patient. In these communications education on the part of the patient is not essential If at all possible, however, intelligent comprehension by the patient of the physician's interrogations is essential. Therefore under all circumstances words must be used, the meaning of which the patient understands The physician must think with the patient and try to understand what the patient wishes to communicate to him It is well to recall that when misused, "words, words, words, are the stumbling blocks in the way of truth. Until you think of things as they are, and not of the words that misrepresent them, you cannot think rightly. Words produce the appearance of hard and fast lines where there are none. . . . Words are the clothes that thoughts wear—only the clothes. I say this over and over again, for there is nothing of more importance. . . . If I could *think* to you without words you would understand me better" (Excerpt, with omissions, from *Anonymous,* quoted by Samuel Butler in *Life and Habit.*)

To follow through with an adaptation from Malinowski: The complaint of a patient is never detached from the situation in which it has been uttered. For each complaint by a human being there is the aim and function of expressing some ...ling actual at that moment and in that situation, and necessary for

some reason or other to be made known to the physician in order either to purposes of common action, or to establish ties which will serve the purpc communion, or else to deliver the complainer of violent feelings or passions. out some imperative stimulus of the moment, there can be no spoken complai each case, therefore, utterance and situation are bound up inextricably with other and the context of situation is indispensable for the understanding of the v Exactly as in the reality of spoken or written languages, a word *without ling context* is a mere figment and stands for nothing by itself, so in the reality spoken living tongue, the utterance has no meaning except in the context of situ

In eliciting the complaint, the simplest, the most natural and, in the en almost self-evident facts are the hardest to evolve and to elucidate and the most cult to interpret. Complaints referring to the primitive fundamental instincts o preservation and reproduction must be carefully listened to, for it is these ins which are so important because they have served to guide mankind in the forn of religious and ethnic systems of moral and spiritual guidance. Often comp are tainted with folkway and folk medicine. Folkway and folk medicine are tially al[illegible]
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moved from belief in supernatural powers which influence the encroachme disease and the fear of death. If most persons are not afflicted with pleasure in the presence of the dead, their parents were. If they have by faith healers, it is the exception and not the rule Complaints o with the doctrines originated by shamanism, including primitive Indian me and charlatanism, or with the patients' own beliefs in herb remedies, naturo
atient has not been t
in one-a-day vitam
eye ball or wear a s
charm, bracelet or finger ring, he may possess these items and secretly rely on in addition to the physician's medicines Such usages are the normal

Every complaint presents at least two components (1) the amount of ph disability present, and (2) the reactions of the nervous system to this disabil in sc

of interrogation
it is unnecessary to question and cross-examine the patient and members c family or friends. Elucidation of many complaints, however, requires though consideration. There are, too, those complaints, apparently definite, whicl patient states clearly and precisely, but which on cross-examination fail to be c significance except to the patient.

Diligence, working theories and hypotheses are occasionally necessary task of eliciting data for a starting point in ascertaining what a patient means complains, "I feel bad all over," who steadfastly maintains this contentior answers normally and satisfactorily all questions pertaining to either the psyc the soma

Complaints can often be separated into those which are purely psychic and those which are purely somatic in origin. Other complaints cannot be definitely classed as either purely psychic or purely somatic and are termed psychosomatic, and finally there are those complaints which are of somatic origin but often colored by the temperament of the patient. It must be emphasized that it is just as important to determine whether a patient is suffering in silence as to know that an overemphasis is being expressed.

Psychic Complaints. At this point in the search for pertinent data in regard to the complaint it is well to digress long enough to define briefly the psychic functions which often are of great importance in the interpretation of the complaint and particularly of complaints which are partially or wholly of psychic origin.

Psychic complaints may occur in two types of individuals: (1) those who by reason of some congenital or protoplasmic fault are mental defectives, or (2) those who have normal mentality and from disease or other reasons become psychically deranged.

Mental Defects. In eliciting a complaint, it may soon become obvious that the patient has a mental defect.

The simple primary amentics comprise idiots, imbeciles and morons of various grades or degrees. In 1934 the American Association on Mental Deficiency (H. M. Pollock reporting) adopted the following criteria for grading mental defect: "An *idiot* is a mentally defective person usually having a mental age of less than 3 years, or if a child, an intelligence quotient less than 20 An *imbecile* is a mentally defective person usually having a mental age of 3 years to 7 years, inclusive A *moron* is a mentally defective person usually having a mental age of 8 to 12 years, or if a child, an I Q (intelligence quotient) of 20 to 49 inclusive.

"As a rule the upper limit for a diagnosis of mental deficiency should be an intelligence quotient of 69, but this limit should not be adhered to in cases where medical, social and other factors clearly indicate that the patient is mentally defective.

"For purposes of this classification in computing intelligence quotients of adults the mental age is to be divided by sixteen The intelligence quotients mentioned above are based on the use of the Stanford revision of the Binet-Simon test "

An *idiot* by definition has a mental age of less than 3 years Such a person, no matter what chronologic age he has attained, cannot be expected to guard himself against physical danger any more than a normal child of less than 3 years of age can do.

Idiots are rarely able to form articulate words In some idiots rhythmic movements, such as swaying or rocking of the body, are almost constantly sustained during waking hours About 50 per cent of cases of idiocy are due to developmental failure in the prenatal period and 30 per cent to birth injury. Idiots constitute about 5 per cent of all defectives

Some idiots are good-natured, others are ill-natured and irritable Idiots often show organic nerve lesions or anomalies in the shape of the skull. About one third of all idiots have epilepsy.

The only difficulty in diagnosis lies in delimiting idiocy from imbecility in cases on the borderline

In *mongoloid idiocy* the child has a peculiar physiognomy, which has led to the name mongoloid There is no agreement as to the etiology of mongoloid idiocy. There are those who believe that the condition is heritable, while others believe, as indicated in the empiric risk of the condition, that it is largely attributable to aging parents

In mongoloid idiocy the face is flat, the nose wide and flat, the malar bones are prominent, the eye-slits narrow and oblique, the eyelids reddened, and the cilia scanty. The cheeks are dull in color with malar prominences flushed. The skull is round, the occiput flattened. The tongue is enlarged and has huge papillae, the dorsum of the tongue is wrinkled and the tongue is often protruded The musculature

is relaxed and soft and the joints can be twisted in remarkable attitudes. The tends to be obese and is very susceptible to infections Many malformations thro out the body have been observed in cases of mongolism These children usuall of infections before they reach the age of 20 years

Imbeciles by definition vary more widely in mental capacity than idiots, for are from 3 to 7 years of mental age They learn to walk, talk, dress themselves follow simple instruction in order to perform simple tasks They can avoid ord physical danger inherent in a simple environment Imbecility originating from fective germ plasm often is accompanied with various physical anomalies and mas of degeneration. About 20 per cent of defectives are imbeciles

Morons by definition more nearly approach the lower limits of normal men than imbeciles They learn to read and write but few attain more than the f grade. If proper supervision is at hand they can do simple routine work The not capable of consistent planning or sustained effort under stress

No better etiologic factors can be assigned for simple primary amentias than alc ism, syphilis, tuberculosis, toxoplasmosis, advanced age of parents, metabolic de consanguinity, toxemias of pregnancy, birth injury, prematurity and morbid here It seems reasonable, however, that a defective germ plasm is the real cause of pri amentia in most instances As cited by Keith in his new *Theory of Evolution*, inbre increases the chances of a defective offspring Likewise inbreeding will make good plasm better

MENTAL DEFECTS ASSOCIATED WITH DEFORMITIES Of the defects of the brum that lead to imbecility may be mentioned hemorrhages, encephalitis, int hydrocephalus, meningitis and porencephaly In some families imbeciles ap singly through a series of generations, suggesting morbid heredity

Mental deficiency may be associated with *microcephaly* In these defective head is of less than the normal size. The condition seems to be due to a defe

[illegible] ... indicator o amount of intelligence which may reside in a very small brain. Most of these chil are delicate and succumb easily to infections.

Microcephaly is to be distinguished from the primary amentias and conge diplegias, in which the head is often somewhat less than the average size, but r so small as that of the true microcephaly

Macrocephaly is characterized by hypertrophy of the brain and by mental ciency It occasionally occurs in more than one member of the same family. Be congenital macrocephaly is so designated, hydrocephalus, brain tumor and c conditions which might cause increased intracranial pressure and enlargemen the head should be excluded. The clinical diagnosis cannot be established wit a complete study of the ventricular system

There is a type of amentia associated with the excretion of *phenylpyruvic in the urine*. The disease seems to be inherited as a recessive characteristic. mental defect is severe. There are muscular rigidity, alterations of posture and tremors and athetoid movements. The diagnosis is made on the basis of urin and the finding of phenylpyruvic acid

The most practical test for the detection of mental defects of these types sists in the lack of ability of the individual independently to meet the world a end of adolescence.

. The parents bring the mentally defective child to the physician and solicit his l in regard to the abnormal behavior they have observed in the child.

A systematic psychic examination of the cognitive, affective and conative funcıns (intellect, emotion, will) is necessary, in order that the mental equipment of e suspected defective may be compared with the average. The possibility of an isting myxedema, cretinism, mongolism or infantilism should always be kept in ind.

Temperament. The peculiar physical character and mental cast of an individual termed the temperament. The temperament of an individual becomes evident in l instances of interpretations of a complaint. Various classifications of temperaents have been offered. All of these have descriptive value but they fail to explain e temperamental differences observed Here two meanings of the term are emoyed: (1) The popular meaning of temperament is disposition The disposition of ı individual implies the natural temper or constitution of the mind, and characteres the individual as amiable or irritable. (2) The scientific classification of temperaents as formed by Kretschmer consists of the cyclothymic and schizothymic or :hizoid types.

CYCLOTHYMIC TEMPERAMENT. The cyclothymic temperament is characterized by ›o contrasting qualities of disposition: (1) cheerful and vivacious (hypomanic) and !) sober and serious (melancholic). The cyclothymes are predisposed to the developent of manic-depressive or affective psychoses. The cyclothymic temperament is often ıbdivided into hypomanic and melancholic types

Hypomanic Temperament. The hypomanic are free from internal inhibitions. They e usually energetic, given to fleeting enthusiasms and easily swayed by new impressions heir judgment is superficial and they have a ready excuse for their failures. They are lept at talking themselves out of difficulties

Melancholic Temperament. The melancholics tend to be easily depressed. They often ‹press regrets and feelings of inadequacy and hopelessness They are preoccupied with ork, feel responsibility, tend to suffer and cry in silence.

A tendency to hesitation, indecision and caution is characteristic of them.

SCHIZOTHYMIC TEMPERAMENT. The schizothymic temperament is characterized by ıcongruities of the feeling-life. In adolescence these individuals are usually willful, ısobedient, headstrong, moody, stubborn, ill-tempered, easily offended and resentful of dvice, supervision or correction The self-confidence which often characterizes these ıdividuals is of compensatory origin and arises from a sense of insecurity.

The sensitive schizoid is lonely, imperfectly understood and isolated The schizoid ; often ambitious, conscientious, meticulous and perfectionistic.

Schizoids may have an imaginative attitude toward life and its experiences, but may ıck the finer sensibilities. They may become cold, reserved individuals who are frequently :alous of those more happily adjusted

Personality Attitudes. Closely allied with the temperament of an individual ıre the personality attitudes which are known as extroversion and introversion, or imply the individual is designated as an extrovert or an introvert.

The direction of interests determines whether or not the individual is an extro/ert or an introvert. The extrovert possesses an abundance of energy which is di:ected to objects and affairs outside himself. He is energetic, aggressive, friendly, sociable and self-confident so long as these attitudes serve his needs The extrovert lacks the delicacy of feeling which is possessed by the introvert.

The introvert may possess the same amount of energy as the extrovert but it is directed toward himself, although not in the sense of selfish advantage at the expense of others The introvert often seems cold and aloof. The introvert tends to be serious and sensitive and frequently is lacking in self-confidence and boldness of activity. Some introverts masquerade under the guise of the extrovert. In such a conversion the introvert may overcompensate and become overbearing and domineering The definite types of personality attitudes predispose to certain mental illnesses, for in-

stance, the extrovert is predisposed to an affective or manic-depressive reaction; introvert may develop schizophrenia

The complaint which the patient makes to his physician may be revealing o defect in temperament

Psychopathic Personality. If an individual possesses mental inadequacies a deviations which are neither psychotic nor feeble minded, and if these aberrati render him unable to participate in satisfactory manner in social and cultural re tions with those about him, the condition is known as psychopathic personality.

Psychiatrists define various types of psychopathic personalities, for instance, stable, excitable, impulsive, egocentric, liars, swindlers, antisocial and quarrelso (Kraepelin) Here, however, mention will be made of pathologic liars and swindle antisocial personalities, sexual psychopaths and persons with situational psychos

Pathologic liars and *swindlers* are of agreeable manners and optimistic. Th select as their dupes the credulous with whom they make social or business conta They distort facts about themselves concerning their own attainments and kno edge in order to profit at the expense and humiliation of their victims The credul individuals, for example maids and matrons alike, often are blackmailed for sex fenses Money and sums from other sources may be obtained by the swindlers su posedly for investment purposes The pathologic liars and swindlers are unsta and are incapable of accepting responsibility or are unwilling to do so

The individual who has an *antisocial personality* is affectively cold and has acceptable, constructive expression of the striving functions He or she rarely fe remorse at offenses against person, property, society or law Many take pleasure a feel pride in their ability to offend moral, religious and legal standards

Sexual psychopathy is manifested in some by an abnormal sexual goal, as homosexuality, and in others by the gratification of the impulse by abnormal metho as in sadism, masochism and exhibitionism

Many of the so-called *situational psychoses* represent schizophrenic, affective paranoid reactions which occur under circumstances involving great emotional d tress, and they thus represent attempts to escape from the hard and uncompromisi reality of some specific, difficult situation Frequently situational psychoses are the nature of confused states or paranoid episodes, or of attacks of irritability, e citement or depression

Patients afflicted with the difficulties described may complain of them, or th may try to conceal their difficulties, and the complaint may be made by others. Lik wise in any of the psychoses the complaint may be expressed by the patient or ma by the family or friends of the patient

Complaints of the abnormalities just described are less likely to be made by t patients than by relatives, by those duped or by officers of the law

Character Disturbances and the Psychoses. The psychic functions in m have evolved from development of the simple instinctive tendencies In each instin tive tendency there are the constituents of knowing (cognitive), feeling (affectiv and striving (conative). Feeling and striving are considered as character, as co trasted with cognition and intellect The intellect seems to be an instrument whi has been evolved in order better to satisfy man's desires by activities through kno ing. In order that a human being may know how to adapt and respond to the eve changing forces of physical and social environment, there must be ever prese adequate cognitive, affective and conative functioning of the mind

Complaints of psychic origin often represent faulty technics of adjustment, ne rotic compromises with reality, and the results of various protective and safe devices employed by the patient in order to serve the ends and aims of the perso ality. In order to understand the complaints of a mental disorder, one must have a understanding of the forces that have gone into their formation, as a means to likely ascertaining what the patient is reacting to and expressing in his com

certain instances the services of the psychiatrist may be required for a full ›oration.

Knowing (Cognitive) Defects. Complaints originating as a result of disturbed ctions of cognition and intellect are referable to (1) the sense organs, (2) the rons of peripheral nerves which conduct impressions through the central nervous em to the higher centers of integration, and (3) the integration and combination hese new impressions with old ones to form perceptions and judgments that are agreement with objective reality How far a given human being, the patient, is lthy or ill and the reason therefore depend on the degree of disturbance of the chic and the somatic functions. It is desired to determine how far the patient is able or incapable of making adequate responses to the psychic and physical uencès of the environment in which he lives

THE SENSE ORGANS The nerve beginnings in the organs of sense, namely, the s, ears, nose, taste buds, touch spots in the skin, and the nerve beginnings in the scles, bones, joints and viscera are essential to the functions of knowing.

The various end-organs, or receptors, are so constructed as to analyze the en- onmental energy and select certain kinds which are transformed in the receptor l give rise to a nervous impulse On arrival in the appropriate preordained area the brain this impulse produces a visual, auditory or other sensory image, the erpretation and meaning of which will depend on the previous experiences of the erpreter The elements which are likely to lead to misinterpretations of these ages, with resulting illusions, are deeply intense affective states or strongly urgent ves and impulses. A misinterpretation of normal stimuli arriving at the higher nters of integration is an *illusion*. The nature of illusions is likely to be determined the prevailing trend of the patient's preoccupations. In confused, toxic states ual perceptions are more likely to be misinterpreted than perceptions involving ier senses because the sensory stimuli and impressions are not sharply defined; s the common occurrence of visual illusions in alcoholic and other intoxications

A more serious falsification of perceptions is the formation of image symbols en there is no discoverable impulse created by the stimulation of a receptor. A ntal image projected outward as a perception in the absence of an external stim- is is an *hallucination*. An hallucination lacks a basis of reality It is created by the tient's own mind, but it constitutes an actual part of the mental life of one thus ected.

The content of perceptions in hallucinations is so intimately subjective that the tient cannot ignore them They absorb the attention completely and reality is ide to harmonize with them The nature of the material hallucinated is influenced the psychologic experiences of the patient.

During the early and acute stages of a toxic psychosis hallucinations are more irked and may be of no great importance in these disorders The hallucination iich occurs with a clear mind is of serious diagnostic import. Hallucinations are equent when attention slackens and there is time for daydreaming

In hallucinations the images are cast in that sense best fitted to symbolize them allucinations of *hearing* are most frequent Feelings of guilt, for example, may best expressed in spoken language, and so the patient hears accusing voices. The ices arrange the words in sentences and give commands addressed personally to e patient The commands are often convincing and compelling and may therefore erce the patient to overt acts

In the deliria of acute infectious diseases or of toxic psychoses hallucinations of *ght* occur most frequently. The classic form of mental disease accompanied by sual images is delirium tremens The images are almost always of a terrifying iture

Olfactory hallucinations most commonly represent feelings of guilt and often cur in schizophrenic states.

Hallucinations of *taste* are uncommon and when present they often are associ- :d with hallucinations of smell

Tactile hallucinations are common in toxic alcoholism and cocaine addiction

Sexual hallucinations are almost always limited to schizophrenia. The hallucina- ons pertain to size, shape or the absence of the external genitalia

All of these abnormalities related to the sense organs are likely to be perceptible the patient's complaint, as he tries to express it to the physician

THOUGHT The joining of ideas and the formation of new ones constitute the unction known as thinking. Thought processes may be disturbed in production, rogression and content.

In mental health the stimuli for thought come from environmental reality and hus thought is rational or realistic. In mental disease the production of thought comes from the inner mental life and is not corrected by reality. For instance, schizo- phrenic thinking finds its origin in complexes, wishes, drives and other motivations not recognized by the patient and operates for the purpose of providing substitute forms of satisfaction Thought wanders without correction by realities

Disorders in Progression of Thought. The rate and manner of progression of thought, if revealed at all, are disclosed by the stream of talk. Of course it is expected that during normal small talk for the purpose of entertainment, there may be a lack of logical and coherent sequence of related ideas Beyond this small talk for entertainment purposes there may be disturbances of the stream of thought in which the thinking processes appear to run too quickly and in which at least some ideas are not completed This condition is known as *flight of ideas* In flight of ideas words of similar sound call up the new ideas This new association of ideas is known as *clang association* and may lead to a pun or a senseless rhyme

The opposite to a flight of ideas is *retardation* of the thought processes In retardation the initiation and movement of thought are slow. The patient's thoughts come slowly and are expressed by a slow speech and in a low tone. Retardation in minor degrees may be normal, when fully developed, however, it is observed chiefly in the depressive phases of the affective psychoses but also may be present in schizophrenia.

A disorganization of syntactic structure of thought with a lapse into disjointed phrases or even into parts of sentences is known as *incoherence* Incoherence occurs particularly in schizophrenia, a disease in which the thinking is characteristically dominated by complexes.

When both expression and progression of thought suddenly but temporarily cease, the process is known as thought obstruction, or *blocking* This often occurs in petit mal epilepsy.

When there is a tendency for the associative evolution of ideas which are determined more by affective factors than by logical reasoning, the strongest feeling tones dominate. An idea which comes to have an extreme feeling tone connected with it is spoken of as an *overdetermined* or *overvalued* idea An overvalued idea is an important determinant of behavior. Individuals possessing degrees of overdetermined ideas are frequently met, particularly in scientific circles and religious gatherings

A *delusion* is a false conception of a particular life situation. The trend of a delusion is determined by the prepsychotic personality problems of the patient The sources of these problems may often be found in thwarted trends and drives, frustrated hopes, feelings of inferiority, inadequacies, impelling desires, feelings of guilt and other affective preoccupations.

The psychologic purposes and needs for the satisfaction of which delusions are created fall into groups of well-defined mental mechanisms. For instance, delusions of grandeur arise from feelings of inadequacy, insecurity or inferiority, any conscious recognition of which is prevented by the exaggerated affective components of the

delusion. Delusions of self-accusation may arise from the repression of unacceptable trends and desires.

Unworthy desires, or troublesome and disowned aspects of the personality, when projected as hostility from the environment, are termed a *delusion of persecution*. Delusions of persecution permit a shifting of responsibility. Those in whom delusions of persecution develop have always been too critical, resentful, suspicious, unhappy, lonely, brooding and insecure, from a lack of friends with whom they could share confidences

When an individual interprets the remarks or actions of other persons, although in no way referring to the observer, as being significantly related to himself, and particularly if to him these remarks and actions express accusation or depreciation, the condition is termed *ideas of reference*. In paranoid states ideas of reference represent a projection of self-criticism onto the external world. In depressed states feelings of guilt often stimulate ideas of reference and may contribute to loosely organized paranoid delusions

When repression weakens, memories or ideas which would cause emotional pain, if admitted to consciousness, may give rise to depression. A *depressive delusion* is the rationalization of a sense of depression resulting from unconscious hostile tendencies felt toward innocent persons.

If an individual's attention is abnormally concentrated on his own body so that he is depressed and his thoughts are obsessively preoccupied with some bodily organ which is thought to be incurably diseased, the condition is known as *hypochondria*. Hypochondria often occurs in those who have shown a tendency to evade the responsibilities of life through illness Hypochondriasis occasionally is symbolic, as in schizophrenia, and as such it indicates a serious disorder.

An *obsession* is the result of thoughts which persistently thrust themselves into consciousness against the conscious desire of the patient. Obsessive thoughts may lead to compulsive acts In a compulsive act the patient feels impelled to perform it The act is often elaborate and repetitive so that it seems almost ritualistic.

Phobias are like the obsessive idea. The individual is filled with morbid anxiety and distress which constantly thrust upon him against his own will. Among the common phobias are fears of dirt, of bacteria, of cancer, of crowds or of closed spaces

Relationship to the Complaint If the physician has the confidence of his patient, the foregoing difficulties in relation to thought, if they have been experienced, are likely to be mentioned in the patient's complaint.

MEMORY. The memory may be phenomenally good, *hypermnesia*, or there may be a loss of memory, or *amnesia*, and in many instances there is falsification of memory, or *paramnesia*

Hypermnesia. Normally the impressions which arise from events which arouse the emotions are registered with more than the usual intensity, with the result that there is always a more vivid recollection of details of these events.

Amnesia In instances of physiologic disturbances of neurons from toxins, trauma or degenerative changes there may be organic amnesia Organic loss of memory is due mostly to an impairment of retention, though registration is somewhat affected. In the patient who has psychogenic amnesia the absence of memory is an active, defensive process The patient always is a hysteric who simply refuses to remember.

Paramnesia Paramnesia may be of different forms. 1 In *confabulation* the gaps in memory are packed full of fabrications which are without any basis of fact. Confabulation is observed in Korsakoff's syndrome but occasionally also in senile psychosis 2 *Falsifications* or *illusions* of memory are created in response to affective needs. They are frequently observed in the reporting of past events. In paranoid psychoses this tendency is highly developed 3. In the phenomenon of *jamais vu* there is a false feeling of unfamiliarity with situations that have actually been expe-

·ced These phenomena may occur in schizophrenia, psychoneuroses, epilepsy and in states of fatigue or intoxication

Dementia. Dementia is a permanent, irreversible loss of intellectual capacity. It occurs most frequently in cerebral atherosclerosis and neurosyphilis.

Disturbances of Consciousness Disturbances of consciousness are often associated with the acute stages of toxic, infectious or traumatic conditions and some ·l diseases A patient in a state of *confusion* is bewildered, perplexed and disoriented. The face presents a distressed and puzzled expression

In *psychogenic stupor* there is no suspension of consciousness, but the patient does not move The thoughts are dereistic. In toxic-organic stupor conscious thought processes are suspended

Delirium is usually associated with fever or toxic states. There is a clouding of consciousness, with bewilderment, restlessness, confusion and disorientation, and illusions and hallucinations may occur

Dream or twilight state is an affective disturbance of consciousness in which the patient does not recognize familiar surroundings In response to visual and auditory hallucinations the patient may run away from home or commit acts of violence. When ·l consciousness is regained, the patient may report that he felt as if he were ·ng and will have little or no recollection of events that occurred during the existence of the twilight state Such dream states occur for the most part in hysteria · in epilepsy They may end in delirium, as described, or they may pass into dissociated states, such as fugues and double personalities.

Disorders of Apperception Disorders of apperception occur in mental deficiency, in psychogenic diseases involving intense preoccupation, and in toxic and organic ·· In disturbances of apperception the patient has difficulty in understanding questions and unaccustomed situations and experiences.

Disorders of Orientation If a person does not know his position in reference to time, does not appreciate the situation both as to space and circumstances, and does not understand his relationship to other individuals, he is said to be disoriented. An individual may be disoriented in any one, two or all of these spheres, that is, the time, place or person Disorientation may occur in any mental disease in which there · extensive impairment of the memory

Relationship to the Complaint The patient may be sufficiently aware of these disorders of memory to complain of them, or they may have been noticed by others who will seek the physician in behalf of the patient

Functions of Affectivity or Feeling. THE PERVASIVENESS OF AFFECT The ·ctions of affectivity or feeling consist of the psychic phenomena known as feeling tones, moods and emotions Feeling tones accompany all sensations and ideas and ·e tinged by either pleasure or displeasure, both of which are conducive to states or emotions that may be termed moods Moods usually are prolonged states characterizing persons as having, for instance, a sunny disposition or a grouchy disposi· ·. Moods accompany all of the episodic emotional states of delight, disgust, joy, ·ief, love, hatred, anxiety, peace, anger and their modifications

Pleasurable Affects. Euphoria is a pleasurable affect The individual is imbued with a subjectively pleasant feeling of well-being Euphoria is most frequently observed in general paresis, multiple sclerosis and in some instances of frontal lobe ·mor Euphoria may readily shift to irritability. Euphoria is contrasted with an air ·f enjoyment and of self-confidence which radiates from some normal individuals.

A mood of entrancing, peaceful rapture and tranquil sense of power is termed ·*stasy.* A religious element is an essential part of the state because it permits of detachment from worldly things and the religious tenet of rebirth and thus purifica·n. Ecstasy represents the achievement of the maximum of wish fulfillment. The ·tion is observed in hysterics, epileptics and schizophrenics.

Depression. An affective dejection varying from mild downheartedness to stupor is known as depression. A reactive depression arises from sickness, bereavement, betrayal, loss of property, job or money, and from many other difficulties. Autonomous depressions arise from unrecognized affective factors the sources of which are beyond the patient's capacity for understanding.

Tension. Tension is characterized by a feeling of uneasiness, restlessness, dissatisfaction and expectancy. It is really a manifestation of anxiety.

Fright, Fear, Anxiety and Panic. Fear and fright are mechanisms intended for the preservation of life They are, therefore, comparable to pain. It is possible to abolish pain and fear temporarily and to a fairly predictable degree with certain drugs.

There are no essential distinguishing features between fear and anxiety. When the threat of danger is acute, fright seems to be the preferable term. When a continuous danger impends, it is proper to designate the reaction as one of anxiety.

Of fear in children and primitive man four aspects can be distinguished:

1 The *mimic* or *pilomotor reflex* is characterized by changes in the skin which, especially in animals, lead to a sort of masquerade. In man a lively reaction takes place in the skin under the influence of serious emotion. There may be shakes and vasomotor changes, and the face loses color. There is a feeling of intense cold. In some an unbearable itch and urticaria make an appearance. The skin may desquamate after a few days Spontaneous extravasations occur in face and legs, painful hypersensitivity of the skin, neuralgic pains, general hyperesthesia of the senses of perception, and complaints of cold and pain may be present, and chronic rheumatism may flare up

2 The *flight reflex* is expressed by mobilization of every facility to escape the danger There is an accelerated activity of the sympathetic system, with increased supply of epinephrine to the tissues, increased blood supply, halting of motility and secretion of the digestive organs or, in some cases, hyperfunction such as passage of bowel movements Reactions of the vascular system are prominent. Cardiac palpitations and sudden sthenocardiac pressure are well known. A weak heart may not survive The common distress reactions are gagging, anorexia, nausea and diarrhea Polyuria and involuntary urination are common A latent exophthalmic goiter may be made active Impotence, a feeling of paralyzed sexual functions, alternating drowsiness and sleeplessness often ensue.

3. A sudden stop to this aggressive activity is *panic.* There are a psychic stand against the threatened danger and a somatic mobilization All psychophysical possessions are geared for defense.

4. The popular expression "I was literally scared to death" may actually be termed the *death reflex,* as the clutching of objects in the hand at the time of drowning There is a general paralysis of functions, and cataleptic posture and a stiffening due to fear are present Cataleptic stiffening after great fright is often experienced In some cases disease symptoms which resemble parkinsonism, anxious eyes (proptosis), tremor of the hands, stiffening of muscles (a sort of decerebrating stiffness) ensue

The breathless stiffening of fright may cause in some an attack of asthma, a fear to breathe, not influenced by any therapy A chronic nervous asthma may result. There may ensue a drop in weight from loss of fluid due to profuse perspiration and internal secretory changes Paresthesia of the extremities, hands and feet going to sleep, and acrocyanosis may ensue.

Fear, whether of magic, evil spirits or the dark, is present in most men When resistance is lowered by disease, by shock or by psychic conflict, fear may become rampant Depending on early training of the individual, fear may develop of dark strange places, loud noises, high places, lightning, thunder, and the graveyard on a bright moonlight night

Inadequate Affect. This is emotional dulling characterized by a lack of sensitiveness to those experiences that normally give emotional response. The qualities of gratitude, sympathy, hope, anticipation, grief, regret, pride or shame are partially or completely lost.

Depersonalization. This is characterized by a feeling of unreality and of changed personality. It is a form of withdrawal from reality. The patient feels that he is no longer himself, but he does not feel that he has become someone else. There is a total loss of affective response, everything seems unreal. Depersonalization occurs in depressions, in anxiety, obsessional states, hysteria and in some schizophrenias. It is more frequent in intelligent, sensitive, affectionate, introverted and imaginative types of individuals than in other types.

Relationship to the Complaint. Evidence of abnormality of the affect (feeling tones, moods or emotions), if present, is very likely to appear in the patient's complaint

Conative or Striving Functions. The conative or striving functions of the human being relate to volition or will and action and timed behavior. The normal person strives to attain certain goals The basic or natural aims of this striving are self-preservation, race continuation, acquisition of knowledge and its dissemination, social intercourse and the appreciation of beauty, right conduct and all the will for the good things of life

Attitude is an acquired conscious desire or an unconscious predisposition to react in a characteristic manner toward a given type of person or situation

Disposition is a sum of the individual's tendencies as determined by the affective and conative components of his personality

Aggression is the deep-seated drive or pattern of the personality possessed by an individual who reacts in a positively forceful way Aggression carries the implication of will to power and, too, of hostility and attack. These tendencies may or may not be obviously expressed In the desirable individual the aggressive impulses are sublimated so as to serve to promote constructive forms of unselfish adaptation.

Ambivalence implies a combination of the use of the action sphere and the affective sphere of the personality. In manifest ambivalence the individual may be abnormally impelled by contrary drives

Disturbance of activity comprises states of (1) hyperactivity or overactivity, (2) decreased activity, (3) repetitious activities, (4) automatic obedience, (5) negation and (6) compulsion

In *hyperactivity* the patient is very busy but the activities often are not productive. The stream of talk expresses a flight of ideas. In *decreased activity* there is delay in starting an activity, and once begun, it is executed slowly *Repetitious activities* are variously expressed for instance, a constant repetition of an activity is *stereotypy*, a maintained immobility of position is *catalepsy* A cataleptic form of immobility is frequently observed in schizophrenics and it is termed *waxy flexibility* Schizophrenics perform many different sorts of mannerisms, such as grimaces, repeated gestures, and peculiarities of gait. Comparable repetitious activity in speech is observed A reiteration of speech is known as *verbigeration.*

Automatic obedience may be expressed by command automatism in which suggestions or requests are compulsively followed There may be a repeating of words or phrases which is termed *echolalia* When words, phrases or movements are initiated without command, these acts are termed *echopraxia.*

Negativism is a refusal on the part of the patient to do what is desired of him or is the performance of the opposite Extreme negativism is characterized by mutism, refusal of food, noncompliance with requests and resistiveness.

It may be a difficulty with the conative, or striving, function which causes the patient to seek the help of the physician If so, at least a hint of difficulty may be found in the complaint which the patient makes.

The Manic-Depressive Group of Psychoses. This is a group of psychoses characterized by manic states (manias), by depressive states (melancholias) or by mixed manic-depressive states. In some cases the patients suffer from only one attack, either of mania or of melancholia; not infrequently there is a regular recurrence (cycle) of the two opposite states of mania and melancholia, the single cycles repeating themselves, after shorter or longer free intervals, throughout the whole lifetime—cyclothymia.

THE MANIC PHASE. In the manic phase of this psychosis the patients experience and manifest an exalted mood; they tend to sudden changes in humor, to flight of ideas, to easy distraction of the attention In the exaltation everything is easy for the patient. The facial expression is happy, though subject to rapid change to anger. There are rapid changes in the direction of the ideas; the patient seems unable to hold an idea in mind, objects about him quickly altering the flow of ideas. There is a tendency to make rhymes, puns and alliterations. The pressure of activity exhibits itself as a preternatural loquacity, or in a tendency to excessive busyness, in the *writing of many letters, in the sending of many telegrams, in the making of unnecessary* purchases, in unnecessary traveling or visiting. Such patients are prone to indulge in sexual and alcoholic excesses

Mild forms of mania sometimes go unrecognized. The patients are often thought to be unusually healthy and vigorous. Once the patients are under observation, the superficiality of it all is easily recognized: the poverty of the underlying thought, the tendency of the mental associations to be influenced by sound, similarity and contiguity, the resemblance to mild alcoholic intoxication, and the absence of insight into the disease.

In the severer forms of mania there may be delusions of grandeur and of extravagant self-appreciation. The mood changes suddenly, without warning there may be an increase of irritability or an outbreak of anger and violence. The patient may attack the surroundings and explode into blackguardism. Patients of this type gesticulate, dance, yell, tear up their clothes or pull out their hair. In the severe forms of the disease they may eat, drink or smear themselves with urine or feces. Under all this maniacal excitement they experience no feeling of fatigue.

*In milder psychoses the orientation may be good, but in the severer forms, espe*cially those with many hallucinations, there are disorientation and confusion.

The patients lose weight rapidly from insomnia, lack of food and excessive movement After several months during which remissions and exacerbations occur, the patients may gradually improve, regain their weight, and return approximately to normal.

The manic states have a marked tendency to recur The first attack usually appears in youth

A maniacal attack of the manic-depressive group must be distinguished from (1) the maniacal attacks in dementia paralytica, (2) catatonic states of schizophrenia, and (3) hallucinatory confusion, or amentia

THE DEPRESSIVE PHASE The depressive phase or melancholic state of the manic-depressive psychosis is characterized by a pathologic sadness and a slowing of thought and emotion, associated with ideas of self-depreciation, ideas of poverty, ideas of sin and hypochondriacal ideas There is always danger of suicide. Digestion is disturbed and the bowels are constipated In the milder states the patients admit that they are sick, in the severe states they deny that they are sick, and may assert that they are just sinful

A large part of the involutional psychoses (senile, presenile, and climacteric psychoses) take the form of melancholia

The psychomotor retardation is the clue which distinguishes depressive phases of the manic-depressive psychosis from other forms of depression. The depressive phases of the manic-depressive psychosis must be differentiated from (1) depressive

phases of dementia paralytica, (2) depressive catatonic states and (3) depressive stages of senile dementia

Mixed Manic and Depressive States Not only are depressive symptoms prone to alternate with symptoms of exaltation, but states are met with in which some of the manic symptoms are combined with some of the depressive symptoms.

Relationship to the Complaint The patient's manner and speech when he makes his complaint often betoken one or the other of the states described, in great or slight degree.

The Paranoid States. By a paranoid state is meant a form of mental disturbance in which delusions, often systematized in character, and, especially, delusions of persecution and of grandeur, develop, with or without hallucinations.

A paranoid state may develop acutely, or it may develop and grow into a system, with progressive increase in delusions

The acute paranoid states are common in chronic alcoholism, taking especially the form of the acute jealousy-insanity. A similar jealousy-insanity sometimes develops in the puerperium or during lactation.

In the chronic paranoid states there are anomalies both of the intellect and of the emotions The disease develops so slowly that for many years a psychosis may not be suspected The patient is often hypochondriacal, retiring and suspicious, and suffers from ideas of reference Later, ideas of persecution appear, such as that people treat him badly, have it in for him, and are trying to poison him. Egocentric, grandiose ideas usually develop, such as ideas of unusual personality and powers, revelations from God, royal descent, ideas of reform and of discovery. In some cases hallucinations, voices and visions are prominent.

According to the nature of the delusions, the paranoid states are described as erotic mania, religious mania, political mania and jealousy mania. Paranoiacs are often homicidal

Most cases can be placed in one of two groups: (1) true chronic paranoia and (2) dementia paranoides In the latter the course is much quicker, the delusions are more nonsensical, and a high grade of confusion and dementia may soon appear

If the patient complains of being persecuted or if any of the other characteristics mentioned are evident in what the patient complains of, the physician should suspect the existence of a paranoid state—but he should not jump to the diagnosis

The Schizophrenic Psychoses (*Dementia Praecox*) The schizophrenic psychoses are often termed the psychoses of adolescence (dementia praecox), a group of mental anomalies presenting marked individual variations, but all having in common (1) development about the time of puberty or at any rate in the first half of life and (2) termination, sooner or later, in a dementing process of variable grade Not all reach a high grade of dementia, in some cases there is arrest with defect; in a very few cases there may be complete recovery. The cause is unknown.

In diagnosis the episodic states are less important than (1) the motor symptoms and (2) the development of a progressive dementia in youth.

Among the variable clinical divisions of these adolescent psychoses, three main types may be distinguished. (1) hebephrenia, (2) catatonia and (3) dementia paranoides

Hebephrenia. An enterprising youth, at puberty, or soon after, begins to stand still or to change his occupation frequently, has an exaggerated idea of his own importance, tends to occupy himself with the deepest problems of existence, shows pleasure in resounding phrases and dry proverbs, or abnormally devotes himself to puns and to practical jokes. Signs of feeble judgment soon appear. Victims of this disorder write long theoretical treatises, publish impossible books or undertake impractical careers Among the complicating episodic states may be mentioned sudden depression, excitation, anxiety or suicidal tendency. Each episodic state is followed by deterioration and by increase of apathy.

The disease usually goes unrecognized for some time, and is designated neurasthenia or hypochondriasis. Hebephrenia should be suspected in young persons with good memory and comprehension who exhibit loss of initiative, dulling of the higher feelings or a sense of failure of intelligence, particularly when no special cause for exhaustion is demonstrable and when the symptoms are not easily got rid of by general hygienic measures

CATATONIA. One of the commonest forms of insanity in young persons is that characterized by (1) specific catatonic phenomena such as negativism, command-automatism, stereotypy, grimacing, anomalies of speech and writing; (2) episodic states of stupor or excitation; and (3) a termination in dementia.

After a brief period of mental depression at the onset, the patients suddenly begin to behave in a surprising manner. Without apparent cause they may suddenly refuse to take food, or they may remain away from home without cause, or they may enter upon some "impossible" marriage engagement. Sooner or later, symptoms of catatonic excitation develop. In a few cases the patient attempts or commits suicide early in the disease, the family not having suspected the existence of a psychosis.

In catatonic stupor there is a peculiar alteration of psychomotor innervation, including negativism, in which the patient shows resistance (1) to any external influence on his will, and (2) to spontaneous motor impulses arising in himself, manifested by refusal to speak, to show the tongue, to take food, to swallow saliva. Muscles once innervated may retain their innervation, giving rise to the so-called stereotyped attitudes such as inclined head, crossed legs, snoutlike projection of mouth and turned-in thumbs. These attitudes may be maintained for hours, days or weeks, despite discomfort or ulceration from pressure.

In command-automatism, on the contrary, there is, in contrast with negativism, a preternatural suggestibility in the motor domain exhibited as waxy flexibility, echolalia and echopraxia.

In catatonic excitation violent, purposeless movements are made, often with loud cries and attacks on surrounding people; sometimes there are suicidal attempts. The so-called monotonous, or stereotyped, movements such as rhythmic swaying of body, rubbing of hands, movements of tongue, are kept up for hours or days at a time, and represent a transition stage between catatonic stupor and catatonic excitation

In intervals between excitation and stupor, certain peculiarities of behavior usually remain, such as grimacing, motiveless laughing or crying, coprophagy, peculiar writing, tendency to verbigeration, irrelevance and mannerisms. On the psychic side there are (1) a slow enfeeblement of the judgment, though the recording faculty and the memory may be good, (2) a dulling of feeling and apathy, (3) sometimes delusions, and (4) an incalculability and bizarreness of behavior.

Certain somatic signs may coexist· exaggerated reflexes; heightened mechanical excitability of muscles and nerves, increased secretion of sweat, sebum and saliva; amenorrhea, subnormal temperature, and remarkable variations in body weight. Remissions and exacerbations are common.

The catatonic phenomena, alone, do not suffice for the diagnosis of schizophrenia, for they are met with temporarily in other psychoses. The combination with mental enfeeblement is essential. The differentiation from dementia paralytica, epilepsy, hysterical twilight states or amentia is usually easy. In imbecility and idiocy the patients have been intellectually feeble from early childhood, whereas in dementia praecox there is a demonstrable deterioration of the mental powers The differentiation from a manic-depressive psychosis is not always easy, but the apathy, the negativism and the evidences of actual mental deterioration will usually be decisive.

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Acute Hallucinatory Confusion (Amentia, Acute Confusional Insanity, Acute Hallucinosis). In various infections, intoxications and states of exhaustion, especially after surgical operations, an abnormal mental state may appear, characterized by (1) the sudden onset of dreamy clouding of consciousness, (2) numerous, and very lively, disconnected hallucinations and delusions and (3) peculiar motor symptoms, consisting either of increased impulse to movement or of stuporous inhibition. The patients are confused, disoriented and incoherent; the recording faculty is markedly disturbed; the mood is anxious and variable. Some of the psychoses of pregnancy and of the puerperal period belong here. The patients usually emaciate rapidly, and they suffer from anemia, anorexia and insomnia

Amentia usually lasts from 6 to 9 months, or even longer than a year. Many die from inanition or from complicating infections; some commit suicide; about one third recover; a few go over into chronic mental disease.

Acute hallucinatory confusion is to be distinguished from (1) manic-depressive states, (2) epileptic insanity, (3) catatonic form of dementia praecox and (4) *dementia paralytica*.

Relationship to the Complaint. These manifestations are likely to be unrelated to the complaint which the patient originally made but may be related to those of a relative or guardian of the patient when the physician is called to meet a frightening emergency.

Psychoneurosis. Without a clear conception of the meaning of the complaint a practitioner of any form of the healing arts cannot fulfill the first obligation to the patient. This obligation is a correct diagnosis. In order to evaluate and assign a specific connotation to many a complaint or complaints a wide familiarity with organic and psychogenic illness is required. For it must not be forgotten that a psychoneurotic illness renders no immunity to organic illness, and likewise an organically ill patient may have and may have always had a psychoneurosis. The psychoneurosis may cause a very great difficulty in the interpretation of the complaint, for the somatic and the psychologic components in any given complaint must be disentangled. Until the somatic and the psychologic components have been separated it may not be possible to determine whether an illness is primarily or wholly psychogenic or whether it is somatic with coexisting psychogenic factors.

Emotional factors play a predominant role in the production of a psychoneurosis. These factors usually have begun to operate in early life and often are manifested by such disturbances as sleep walking, crying out in sleep, enuresis, disturbances of speech, food idiosyncrasies, delirium accompanying slight rises in temperature, destructiveness, emotional excitability, tantrums, phobias, compulsions, shyness, nail biting and other behavior affections.

In the psychoneuroses the personality remains socially organized. It does not deny the existence of reality, it attempts to ignore it. The interpretations of the environment remain unchanged, although certain elements are given abnormal affective values Repression is maintained, but the repressed material returns in a distorted form so that it is acceptable only to the patient.

It seems that many persons are unusually sensitive to the tension and conflicts of life and react to these with faulty reactions which impair the efficiency of the individual. These faulty reactions often create anxiety, which is one of the commonest and most important sources of psychoneurotic disorders. Anxiety disturbs physiologic functions In acute forms anxiety may produce spasm of the cardiac and pyloric portions of the stomach, intestinal spasms, hyperchlorhydria, diarrhea or constipation, palpitation, tachycardia, extrasystoles, vasomotor flushing and increase in body temperature (99 to 100 F) and respiratory distress The hands and face perspire The patient may have fidgety movements of hands or feet, the voice may be uneven or strained and the pupils may be widely dilated. Anxiety, therefore,

DEMENTIA PARANOIDES Dementia paranoides is an adolescent psychosis w is observed less commonly than either hebephrenia or catatonia. It is characte by a rapidly advancing delusional state in which the delusions quickly become surprising and nonsensical, terminating ... feeble-minded ... and are ... depression and excitation

At ... depressive symptoms usually predominate (insomnia, self-accu tion, "blueness," unrest, suspicion, sense of change in the environment) and id of reference prevail Illusions, hallucinations and delusions soon appear, the l consisting chiefly of grandiose, or of ... rapidly the ... The g ... characteristic, suggesting that of demen paral ... delusional falsifications of memory are common; the patient tells stor of marvellous experiences or of wonderful personal acts

There is no disease-insight. The apathy and indifference are characteristic. T dementia progresses rapidly with the appearance of incoherence in speech a writing

The diagnosis may be difficult at first, but is easy later on The condition mu be differentiated from (1) chronic hallucinatory paranoia and (2) dementia par lytica The age, somatic signs, and findings in the cerebrospinal fluid will elimina syphilis of the nervous system

RELATIONSHIP TO THE COMPLAINT. The complaint ... by a victim of schiz phrenia is likely to be ... given by the patien may lead the phys ... the history or signs

The Infectious, Toxic and Exhaustion Psychoses. Under this heading are listed the initial deliria, febrile deliria and convalescent deliria of the infections and intoxications. In infectious diseases, delirium may appear at the beginning or during the main course, or in convalescence. These forms of delirium may occur in the course of any infectious disease There need be no relation between the height of the fever and the intensity of the psychic symptoms

FEBRILE DELIRIA In the febrile deliria the principal symptoms are (1) clouding of consciousness, (2) disorientation, (3) hallucinations, in addition, there may be (4) violent motor excitement, sometimes resembling that of mania, or (5) stuporous states

DELIRIA OF CONVALESCENCE The deliria of convalescence may appear suddenly, after the temperature has become normal They consist of (1) dreamlike confusion, (2) hallucinations and illusions, (3) occasionally delusions and (4) lively motor excitement The patients are usually anxious, and suffer from self-accusation, ideas of sin and other micromanic delusions, sometimes, instead, the state may be euphoric Stupor and excitation may alternate The outcome of these deliria is usually favorable

COMA, SEMICOMA, STUPOR AND CONFUSION *Coma* is a state of complete unresponsiveness to the environment The patient's reactions are limited to elemental reflexes, and even some of these are impaired *Semicoma* is a condition in which there is responsiveness to some of the elemental mental functions ... y name, reacting to noise and reacting to a ... t in the elemental reflexes ... in which ... execute f ... tongue *Confusion* is a s ... disturbance in the state of consciousness. The st ... elemental mental functions and reactions to simple commands are usually intact These patients present chiefly orientation difficulties.

in lies. They do not intentionally lie; this lying is but the pathologic phenomenon due to faulty reproduction. This faulty reproduction or transformation of memories is the so-called pseudologia fantastica or mythomania. These patients may have a complete but transient amnesia, or the amnesia may concern only persons or events

The feelings of the hysterical individuals are easily hurt. These individuals believe that they are misunderstood; they think that others do not pay them the attention that is their due or that others intentionally slight them.

Many hysterical patients may be unable to eat, or they vomit almost constantly, a condition termed anorexia nervosa. In others the abdomen may be continuously distended with gas, and this is termed hysterical meteorism, or the patient is called a bloater. In a few patients there may be a retention of the urine. A rare form of the disease is pseudocyesis; the patient, even without exposure, may think herself pregnant.

There may be transitory disturbances of consciousness such as hysterical twilight states, somnambulisms or trances The hysterical twilight states appear suddenly. There is confusion and silly childish behavior resembling simulation, and the condition may last for hours, days or weeks.

The hysterical trances, or lethargic states, may be characterized by sleep for days, weeks or months, though enough consciousness may be maintained to enable eating, drinking, voiding and defecating If aphasia is present, the patient may not have any difficulty in communicating in whispers The hysterical mute can communicate freely and correctly by writing.

Standing and walking may be difficult or impossible for the hysterical patient When the patient lies down, no disturbance of motility, sensibility or co-ordination can be made out. Some patients who cannot stand or walk can crawl or can swim. The condition is commoner in women than in men, and in young people than in old. It was formerly termed astasia-abasia There may arise a complete immobility on account of pain, although no cause for the pain is discoverable. The symptom is an hallucination in the pain sense Some of these patients during the attacks of pain manifest tachypnea and tachycardia.

The Ganser syndrome is a paralogia. It has been frequently present among prisoners of war awaiting trial As in many other hysterical states the hysterical protection from a full realization of the true situation affords a relative freedom from the anxiety which might otherwise be intolerable.

The recognition of hysteria is usually easy through the characteristic stigmas and through the exaggerated, often theatrical, character of the mental symptoms and the capricious, oscillatory course A hysterical patient also can have an organic disease.

Accident Neurosis (*Hysteria*) In persons of a paranoid tendency, those who are insecure, those who crave sympathy and attention, and those continuing work beyond mental or physical capacity, unpaid financial obligations or the failure to derive satisfaction from work all may predispose to a traumatic neurosis. The conviction on the part of the patient that there is the right to expect compensation may be a motivating factor. A period of time between the injury and the appearance of the mentally determined symptoms which is occupied with vague affective disorders often supervenes.

The symptoms of the accident neuroses, except in the matter of compensation, differ in no essential feature from those of other neuroses In those cases in which compensation is a participating motive, the patient remains unaware of such an influence and denies the desire for compensation Underlying feelings of guilt may be overcompensated and experienced as self-pity.

Occupation Neurosis. In occupation neuroses the patient, on attempting to execute some specialized movement performed in an occupation requiring the co-ordination of groups of muscles, suffers from a spasm of the muscles involved in

together with the various mechanisms developed to avoid it, constitutes an important factor in the development of psychoneurosis.

The psychoneuroses are said to be more frequent in women than in men. This is probably a matter of degree and sex of the author rather than of incidence. Therefore it is not well in diagnosis to infer that the numbers of psychoneurotic women greatly exceed those of psychoneurotic men, for they do not, and there is no reason that such should be true

Most neuroses of adults develop between late adolescence and 35 years of age. This is the period when the individual becomes confronted with the problems of adult adjustments and responsibilities It is the period when satisfying social, economic and sexual situations should be established. Frustrations in these fields may lead to conflict, anxiety and tension that are met only by neurotic mechanisms.

Hysteria. Hysteria is characterized by an abnormal mental state in which there is a disproportion between affective reactions and the stimuli that give rise to them. The suggestibility of the patient is heightened; the sudden transformations of the emotional states and the moods are best described by a marked degree of caprice

The disease is much commoner in women than in men It begins in adolescence, sometimes in childhood Most patients have a distinct infantilism in the psychopathic field Provocative causes are fright, anxiety and trauma.

Hysteria may begin with a feeling of constriction in the neck, or as a lump in the throat which cannot be swallowed, usually associated with loss of the pharyngeal reflex, and clavus hystericus, or pain in the region of the large fontanel, described as resembling a nail being driven into the head. Hysterical paralyses include hemiplegia, monoplegia, aphonia, astasia-abasia, ptosis and retention of urine Hysterical blindness and agnosia may be present in some instances.

Hysterical hyperesthesias include the so-called spinal irritation, or tenderness, on tapping the spinal column, ovarian tenderness on pressure in the region of the ovary, and various hyperesthetic zones occurring in any part of the body. Vasomotor and secretory lability is often expressed in hot and cold flushes and localized disturbances of sweating.

Hysterical convulsive seizures occur in which patients, without injuring themselves, sink down and assume, and maintain for some time, remarkable attitudes, such as the arc of a circle, or various pathetic or theatrical positions, or exhibit wild, rotating movements The attack can be terminated by a dash of cold water. The more common hysterical seizures include silly laughing, crying, coughing, hiccough, torticollis and muscular cramps.

Hysterical anesthesia may affect one extremity, one half of the body, or two extremities simultaneously, becoming ever more marked the more attention it receives. Often the anesthesia has a topographic distribution corresponding to areas of skin covered by certain articles of clothing such as the gloves, chemise, drawers or stockings. Exaggerated reflexes with false ankle clonus may be present.

The principal mental stigmas are a pathologic lability of mood, fallacies of memory, ideas of reference and lack of consideration for others

The hysterical patient is abnormally irritable; slight annoyance may lead to explosive behavior, and thus the expression, "he became hysterical" It sometimes seems as though the smallest stimulus excites the greatest reaction. The smallest and seemingly most insignificant incidents may give rise to convulsions and twilight states However, in an emergency the hysteriac may exercise a great calmness of action. The hysterical [illegible]
and the next moment, [illegible]
suspicious and sullen. [illegible]
periods, at the menopause and during pregnancy than at other times.

Hysterical patients are incapable of objective report. Often they seem unable to distinguish what they remember from what they imagine. They are thus often caught

Since the patient is perfectly sane, his complaint often is thoroughly descriptive.

Neurasthenia. Psychiatrists believe that the cause of neurasthenia is mental, and they no longer believe that a generally impaired or exhausted physical state in which the nervous system is drained of its energy is ever the cause of this disorder. In general diagnosis and the general practice of medicine a greater number of patients will be found who are physically exhausted and who do recover from the so-called neurasthenia after rest and success, than the number whose symptoms are due to a purely mental disorder such as repressed hostility, constant failure, frustration, disappointment, boredom and monotony

In neurasthenia there are a sense of mental and physical fatigability, tension, irritability, painful and other abnormal sensations and depressive affective tendencies. There may be complaints of dizziness, of a feeling of pressure on the head and perhaps of pain in the back of the neck. Often there is an intolerance of noise, bright lights and cold Gastrointestinal complaints such as gas, indigestion, constipation and diarrhea are common. Often the skin is flushed and sweating. In men an impaired potency and failures at intercourse may occur. Advancing age, not neurasthenia, is the usual cause of failures at intercourse in men who are more than 50 years old.

In the morning the patient awakes with a feeling of exhaustion, but as the day progresses there is improvement and by evening there is comparative freedom from the exhaustion. Many patients are shy and awkward and lack confidence in themselves They may be critical, dissatisfied, envious and resentful and may appear to take pleasure in finding fault with and annoying others

Psychoneuroses usually if not always show mixed features. It is most important to distinguish neurasthenia from the depressive form of manic-depressive psychosis and early schizophrenia These differentiations are made, by the psychiatrist, through time and observation

Relationships to the Complaint. The complaint voiced by the patient often is of diagnostic importance.

Hypochondriasis. Hypochondriasis represents a faulty type of adaptation to personality inadequacies with which a sense of disappointment or of guilt is associated T[illegible]
or bodil[illegible]
persons [illegible]
proportions The patient complains of these things.

Pain. Pain is of primary concern in most complaints The evaluation of pain in the complaint aids in diagnosis and management of the patient Pain is a sensation like smell, taste or vision It can be further compared to these sensations, for it is first a sensory perception This sensory perception is the pain threshold Pain has a reaction which is usually unpleasant but not always so. However, the important conception of diagnostic value of pain is the fact that sweating, tachycardia, digestive disturbances, anxiety, fear, terror, panic and prostration may be solely reactions to pain

Pain is a centrally integrated experience, the painful sensations being derived from impulses traversing specific pathways. According to Wolff and Hardy all fibers carrying impulses experienced as pain enter the spinal cord through the dorsal root ganglions After entering the cord these impulses are conveyed across to the opposite side, where the pathways are localized in the anterolateral portion of the spinal cord The fibers of the spinothalamic tract pass into the nucleus centralis posterior of the thalamus The cortical projection from the nucleus centralis posterior is predominantly to the postcentral convolution. It is probable, according to Wolff and Hardy, that the brain structures involved in pain perception occur in both hemispheres in the region of the central fissure.

The dual aspect of pain, that is, the distinction between perception and reaction

this act. The function of the muscles remains unimpaired when the same muscles are employed for the performance of some other act.

RELATIONSHIP TO THE COMPLAINT. In the complaint which the patient makes, he often reveals to the physician the hysterical nature of his underlying condition.

Psychasthenia (*Compulsion Neuroses*). Psychasthenia includes phobias, obsessive thinking and compulsive acts.

A *phobia* is a fear or dread associated with an idea, object or situation. Among the common phobias are fear of dirt, of bacteria or of certain animals. To many of these ideas, objects or situations Greek prefixes are applied, and thus are produced such terms as claustrophobia, the fear of confined spaces The phobic patient cannot avoid these fears, and if forced into an anxiety-producing situation, a state of agitation follows, the patient cries and shakes all over, may have general tremors and be unable to continue the duty at hand, and may become overwhelmed with panic

A phobia is often a fear of disease. Reassurances that somatic disease is not present often accomplish much in some patients. In others such assurance is of no value

Obsessive thinking is defensive in purpose. Distressing thoughts are composed of contents repugnant to the individual's conscious moral and esthetic feelings In a mild degree these are normal, for everyone has such thoughts, for instance, of tipping over a glass of water on the dinner table when too much formality is being practiced about the table

Obsessive thinking, characterized by persistent doubting, vacillation and indecision, may assume the form of *folie du doute*.

Compulsive acts are characterized by an irresistible urge to perform a certain repetitive, stereotyped act One of the commonest compulsive acts is that of getting out of bed after retiring, to check the gas or electricity or to see if the doors are locked The compulsive act reduces the intensity of anxiety.

Since everyone has defensive character traits, the diagnostic decision must often be arbitrary In the fully developed cases with the well-marked obsessive thinking, fears or compulsive acts, there is of course no question

A failure on the part of the patient to regard his phobias and compulsions as absurd indicates a schizophrenic origin

The depressions of manic-depressive psychosis may be accompanied by obsessive ideas

Anxiety has been defined as a state of heightened tension often accompanied by somatic reactions, usually in the vasomotor sphere It may arise when there is a threat to the personality. Anxiety often arises in association with frustrations related to property, job, money, sex or marital adjustment. The patient usually recognizes the tension and anxiety-producing agent, and often there is nothing that can be done about it.

The anxiety is often expressed by symptoms of depression, irritability, restlessness, psychosomatic disturbances, outbursts of aggressiveness, attacks of weeping and feelings of inadequacy and inferiority accompanied, perhaps, by a paranoid attitude. There may be difficulty in falling asleep, disturbance by fearful dreams, suffering from coarse tremors or trembling. The hands and feet are cold and clammy. The patients are absent-minded. There may be periodic acute, panic-like exacerbations lasting an hour or two These acute attacks take many different forms of representation, such as rapid heart action, precordial discomfort, nausea, diarrhea, desire to urinate, dyspnea and a feeling of choking or suffocation. The pupils are dilated, the face is flushed, the skin perspires, the patient suffers from paresthesias and tremulousness, feels dizzy or faint, and often has a sense of weakness and of impending death. The patient may express beseeching and apprehensive appeals for help.

sensory peripheral nerve fiber or a nerve trunk be injured, the threshold for pain is altered or obliterated. In the central nervous system, the pain threshold is altered or obliterated by spinal cord injuries. Lesions in or near the internal capsule of the brain may elevate the pain threshold.

The most important alterations of the pain threshold to be evaluated in the complaint are those resulting from psychologic factors These factors may raise the pain threshold; for instance during intense emotion, as during fright, severe injuries may be sustained without knowledge. Autosuggestion, hypnosis, distractions, malingering and mental concentrations all raise the pain threshold Anxiety, tension and fear seem to lower the pain threshold A lowered pain threshold is never solely due to structural disorder of the nervous system.

THE LEVELS OF PAIN INTEGRATION IN THE CENTRAL NERVOUS SYSTEM. There are three levels in the central nervous system at which pain may be integrated: the tectum mesencephali, the thalamus and the cerebral cortex.

In the tectum mesencephali the appreciation of pain is no more than a feeling tone and therefore probably is closely related anatomically and physiologically with the activity of the hypothalamus, its powers to perceive pain having been taken over during the process of evolution by the thalamus.

The fact that pain is relatively little influenced by small cortical lesions is the result of the numerous pathways which are provided by the thalamus for the passage of pain sensation to the cortex

The appreciation of pain stimuli at the cortical level is modified by the state of activity of other cortical centers so that the perception may be aggravated in some instances and prohibited in others.

Wolf has named six basic mechanisms which are responsible for headaches of *intracranial* origin These are (1) traction on, and displacement of, the great venous sinuses or traction on the veins that pass to the venous sinuses from the surface of the brain; (2) traction on the middle meningeal arteries, (3) traction on the large arteries at the base of the brain; (4) distention and dilatation of intracranial arteries; (5) inflammation in or about any pain-sensitive structure of the head; and (6) direct pressure by tumors on the cranial nerves containing pain-afferent fibers

The *headache associated with the fever* of acute infections is due primarily to the distention of the intracranial arteries The spontaneous increase and decrease of intensity of the headache of fever parallel the changes in amplitude of pulsations in these arteries The amplitude of pulsation of the cerebrospinal fluid in the headache of fever is greatly increased during the fever. These amplitudes of pulsation of the cerebrospinal fluid during fever headache are in marked contrast to the amplitude of pulsation in migraine, which is not accompanied by such a disturbance It may be that these pulsations account for throbbing headaches of fever

Headache from intracranial hypertension or disease is usually referred pain from the affected intracranial pressure Pain referred to the head from disease of tissue not in the head does not occur. Fever is often accompanied by headache, but this is not referred pain

Headache is a common early symptom of a space-occupying lesion within the skull, sometimes it is the initial symptom The absence of a headache, however, does not preclude the possibility of a space-occupying intracranial lesion. The symptom, headache, as arising from intracranial pressure, always requires assessment.

The headache from a space-occupying lesion, intracranial hypertension, renders the sufferer clearly intensely preoccupied with pain, and the questions and physical examination are but an addition to the burden of the pain These patients observe an economy of movement and of speech, since effort aggravates the pain. The pain is never spoken of as continuous over long periods, since organically determined headache is never so continuous, but always is subject to intermission over varying

to pain, is apparent and is easily appreciated in the case of heat, light, touch, cold and olfactory perception. The reaction pattern of the organism to noxious stimuli has many co[illegible]ponents Reaction to pain is modified by conditioning experiences, such as [illegible]tement of a game or combat, the apathy that accompanies tissue damage [illegible] certain religious and mystic practices, and the indifference to tissue damage during sexual excitement.

Total absence of the usual physiologic behavioral responses to noxious stimuli is rare Ford and Wilkins described three children with lack of reaction to pain rather than absence of pain as sensation They could appreciate light touch and could distinguish between warm and cool test tubes and between the head and the point of a pin. They were, however, indifferent to damaging stimuli Kunkle and Chapman described a young man who had almost complete insensitivity to pain and attacks of unconsciousness beginning in childhood Boyd and Nie described an otherwise apparently normal girl, 7 years old, who was completely insensitive to pain The usual painful responses could not be obtained by any stimulation She was able to distinguish sharpness from dullness, and the senses of touch, vibration, position and agnosis were normal. Boyd and Nie suggested two hypotheses to explain the patient's indifference to pain (1) There exists a congenital structural defect with incomplete neural connections and communicating fibers in the postcentral area with consequent inability to organize the complex concept of pain (2) There is no neurologic defect, but there is indifference to pain, which represents an aphasia-like disturbance

McMurray reported an exhaustive study of a patient with universal insensitivity to pain At no time, during any of the experiments in which noxious stimuli were used, did the patient report a sensation or feeling that could be interpreted as a report of pain Consistent with this was the complete absence of any observable signs of painful experience

Varieties of Pain. Two varieties of pain are recognized, superficial and deep Superficial pain is characterized by the quality of localization and has the components of sensations described as pricking, sharp, burning or itching, it incites the action of fight or flight Deep pain possesses the qualities of a diffuse aching or of a colic It incites the actions of withdrawal, forces a cessation of activity, and causes the affected one to seek protection Deep, severe pain may cause nausea and vomiting

Threshold of Pain. *Pain perception* is the threshold of the amount of stimulus required first to produce a painful sensation. In superficial pain the pain threshold can be elicited by heat, pinprick or chemical agents The threshold for deep pain can be elicited by electric or mechanical means such as a faradic current or the stretching of a hollow viscus The determination of pain threshold experimentally as well as in practice is based solely on the accuracy of the verbal report Despite the inaccuracies of the verbal report, the pain threshold in man is relatively stable and uniform The threshold for the perception of pain is found to be of the same order of uniformity as is the pulse rate, the number of leukocytes of the blood, or the blood pressure. The difference of pain threshold in different individuals lies in the individual reactions to pain. Generally it may be asserted that the alarming experiences aroused in the mind of the patient are the most distressing aspects of pain. For instance, morphine does not discontinue the perception of pain but it does remove the fight-flight-anxiety reaction of the sufferer

The pain threshold, like the other somatic components, may be altered. The pain threshold is lowered by traumatic deformation, denudement, or injury of tissues near the sensory nerve endings responsible for the reception of pain stimuli For instance, a mildly sunburned or a frost-bitten skin is twice as sensitive as a normal skin. The threshold for pain is raised or obliterated by local anesthetization. If a

then is carried, in this neuronic pathway, to the brain, and is perceived as coming from the distribution area of the second neuron.

The most numerous and important of reflected pains are those due to pathologic changes in the internal viscera The viscera of themselves have no sensation of pain, as elicited by ordinary pain-producing stimuli, but when the viscera are irritated, the stimuli are carried to the cord and react on the cord cells, and impulses are produced and sent out as motor impulses or are carried to the brain by the neurons of these cells where they are produced as pain At the same time, the adjacent set of cells become irritable and react abnormally to all stimuli reaching them from the periphery. In this phenomenon lies the origin of the hyperalgesic zones of Head which are responsible for several peculiarities of pain production.

Transferred pain may have varying degrees of two components: (1) The stimulus passes from the neuron in which it is originally present, over an intermediate neuron, to a third neuron, in the area of distribution of which it is perceived as being present (2) In other cases the sensorium mistakes the peripheral distribution of the pain, as in degeneration of the posterior roots (tabes), or of the ganglia and posterior columns or cornu of the cord.

Examples of pain transferred to a homologous segment in the same relative position on the opposite side of the abdomen are found in appendical and ovarian diseases, pneumonia and pleurisy. Examples of higher and lower reference are found in those cases in which the pain of pneumonia is transferred to the appendical region, or in which the appendix causes pain which is transferred to the thorax.

The term crises has been applied, under certain conditions, to paroxysmal attacks of pain of great severity It is accepted that a pain crisis consists of a paroxysm of pain as violent as human nature can endure, accompanied by excessive functional activity of the part attacked, but disappearing as rapidly as it appeared, and that it is associated with a condition of undisturbed functional activity of the affected viscera between the paroxysms.

Tissue susceptibility to pain is determined by the blood supply of the organs. The organs which are the richest in blood supply generally suffer the greatest pain and, with the exception of the bones, the organs poor in blood supply have little, if any, pain

Clinical Evaluations of the Complaint of Pain. Often much time is wasted if too long is spent on inquiries into details of location, situation and distribution of pain, the degree of itching and the occurrence of dizziness as complained of by the patient

Effeminate men and wordy women are inclined to exaggerate in recounting their symptoms A statement made with a cheerful countenance that the speaker is at the moment suffering horrible agony does not square with the facts; the combination of cheerful manner and exaggerated speech is of diagnostic value as indicative of self-deception, hysteria or a habit of chronic overemphasis.

In the majority of cases in which really severe pain is present, certain symptoms are manifest that cannot be simulated. The respiration is increased in rate, the pupils are dilated, the skin is wet with perspiration, the pulse is likely to be tense, there is a feeling of faintness, and frequently a large amount of urine is passed within a brief period after onset.

In the patients' manner of describing pain there are differences that already have been implied Some patients, as a matter of pride, practice understatement of their subjective sensations, whereas others from various motives habitually magnify their suffering and, in most instances, without the slightest intention of deception This mental attitude arises largely from a desire to obtain relief by impressing the physician with its urgent necessity

Variations in descriptions and perhaps in pain sensibility are racial as well as individual Persons of Semitic stock and members of Celtic and Italic groups appear

periods of time if it is of long total duration. Freedom from pain is admitted without emotional difficulty by the patient, and in the periods free from pain an attempt is made to return to accustomed activity (Walshe).

Histamine headaches are primarily due to dilatation and stretching of the pial and dural arteries and their surrounding tissues. The large cerebral arteries at the base of the brain, which include the internal carotid, the vertebral and the basilar arteries and the proximal segments of their main branches, are chiefly responsible. The fifth cranial nerves are the principal afferent pathways for the pain felt in the frontotemporal and parietal regions of the head. The ninth and tenth cranial and the upper three cervical nerves are the afferent pathways for the pain felt in the occipital region of the head.

In *migraine headache,* aberrations in the tension of the extracranial and possibly the dural branches of external carotid arteries may be responsible for the cephalalgia It seems likely that the point of origin of the scotomas of migraine is situated in the cranial cavity.

A *psychogenic headache* is commonly described as continuous and unremitting over long periods of weeks, months or even years. It responds to none of the usual analgesic drugs. This headache is described by the psychoneurotic as terrible, agonizing, as if corkscrews, knives or needles were piercing the head. When questions as to locality and quality of the pain are pressed, the patient's answers become vague, and "pains" are sensations of weight, pressure, or constriction and not real pain at all In the hysteric these accounts are commonly given with animation and evident satisfaction, while the anxiety neurotic is plunged in gloom and self-pity In these patients there is no true pain, but an image of pain conjured up by the patient and subjected to those processes of progressive elaboration to which mental images are prone

It has generally been believed that the majority of headaches *following spinal anesthesia* are the result of leakage of spinal fluid through the dural puncture, with subsequent changes in cerebrospinal fluid dynamics, loss of cushioning effect on the brain and resulting pain owing to pressure or traction, or both, on sensitive brain structures and large vessels

The mechanism responsible for the production of headache after *lumbar puncture* is not clear. At present there is no better theory than that accounting for the headache on the basis of a lowering of spinal fluid pressure by the removal of spinal fluid and loss of more fluid by leakage after the needle is withdrawn

Aberrations in the Central Projection of Pain. *Propagated pains,* which are felt in areas other than those in which they are produced, are classified as associated, referred, projected, reflex and transferred pains. This classification is important to remember when the complaint is evaluated.

Associated pain depends for its production on transference of stimuli from one nerve cell to another. In some cases the means by which the stimuli are transferred cannot be determined.

Referred pain is that class of pain in which the irritation occurs along the course of the nerve fibers, and the pain is felt as being produced in the somatic peripheral distribution of the affected nerve or nerves

Sympathetic pain is really a transferred pain with the distinction that in sympathetic pain a painful sensation is present in the organ originating the pain, whereas in transferred pain there may be no painful impression or sensation in the region or organ in which the pain originates.

Projected pain is felt as being present either in a part that has no sensation (as in locomotor ataxia) or in a part which, because of amputation, no longer exists.

Reflected (deflected or reflex) pain is that pain in which the stimulus is carried to the sensory ganglia or to the cord and then is transferred from the sensory filaments of the neuron primarily affected to those of a secondary neuron. The stimulus

When a patient has a disorder induced by the physician through auto-suggestion based on the physician's examination or manner of discussion of the disorder, it is designated as an *iatrogenic disorder.* A patient may have a disease or disorder induced by the technical procedures employed by physicians and specialists in examinations, medications, or operations; these conditions are designated *iatrotechnical diseases or disorders.*

Experience teaches that each topographic area of the body and each system of the body is liable to iatrogenic disorders or iatrotechnical disorders For instance, locomotor disorders may be induced by the prolonged application of appliances, even if properly fitted Improper fitting of appliances may be disastrous, as illustrated by Volkmann's ischemic paralysis. The use of unnecessary arch supports or the transfer of arch supports from one pair of shoes to a second pair of a different size or last is a common cause of complaint.

The application of appliances, for instance, a stiff heavy back brace for a fatigued back without significant organic disease, may originate a serious disability in a hypersensitive patient.

A bunion operation in an occasional instance may leave a hypersensitive, painful scar just as disabling as the original bunion and thus create an iatrotechnical disorder.

Inquiries by a physician regarding the complaint of cough in association with expectoration, hemoptysis or shortness of breath may initiate these symptoms for

drip fixes the disorder of sinus trouble in the patient's mind, and the postnasal drip is complained of as sinus trouble.

The recognition of the complaints indicative of hyperventilation and that of sighing respirations is more essential in many instances than the recognition of some such condition as a mild pulmonary emphysema If a patient has one of these syndromes, it should be made clear to him that he has an insignificant illness resulting from a nervous tension and not disease of the lungs which prevents the entrance of a sufficient amount of air into the lungs

Perhaps there is no disease any better known and more dreaded by most intelligent patients than is pulmonary tuberculosis At times extensive study and observation may be required in order to determine whether or not the reinfection type of pulmonary tuberculosis is present. If there be indeterminate symptoms present, whether or not these are the result of an active pulmonary tuberculosis, care is exercised lest the suggestible patient become overly concerned before an active pulmonary

the physician in explaining an irritative neurogenic cough, by the time the patient reaches home after having pondered the questions and the examinations made by the physician, often an entirely erroneous conclusion is reached of what has been said The patient reasons that so many questions would not have been asked and so many examinations would not have been made just to explain an inconsequential cough There is no way for the physician to avoid these reactions in his patient except to recognize so far as possible the reactions of certain individuals and avoid any suggestive remarks concerning the organic bases for the complaints until sufficient objective data have been obtained or such data cannot be had.

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to possess an average of greater sensibility to pain than those of Teutonic or Slavonic groups. The important variations, of course, are personal or individual. The neurotic patient of any racial group will complain bitterly of pain from a cause which should not give rise to more than simple discomfort The pain suffered by the abnormally sensitive person, however, is as real and existent in the consciousness as the slight discomfort felt from the same cause by a person given to less verbosity. The pain suffered by an abnormally sensitive individual, even though such pain in a normal subject might not be considered severe, is quite as disabling as a more severe pain in a more stoic individual.

Manner of life and occupation probably do not modify susceptibility to pain. The habitual endurance of hardship teaches the realities of life and trains the individual in the methods of proper evaluation of pain Conversely, the person guarded from rude mental or physical contacts and not accustomed to discomfort and pain, may feel that moderate pain is unbearable. A strong mental prepossession, such as religion, or excitement over an accident, may interfere temporarily with the registration of painful impressions on the consciousness Sensibility to pain is likely to be increased by its long continuance, and it is a common observation that each recurrence of pain during the course of a disease finds the patient less able to bear it. Fright or expectant apprehension invariably increases pain and sometimes originates it.

Complaints Referable to Iatric Disorders. The impression is often gained from eliciting the complaints of patients that they have got the terms, definitions and expressions used in descriptions of their discomforts from observation or discussion with others who are sick or ailing In some instances they have acquired their terminologies from physicians.

Information, terminologies and misinterpretations gained from talking to relatives, friends or other patients are not nearly so serious as those obtained from physicians or from others who administer to the sick and indigent When a patient goes to a physician, this act is in itself an expression of confidence in that physician. Whatever the physician tells the patient, the patient believes in most instances Since the patient believes the physician, this places a responsibility on the physician to mark his words when discussing a patient's disease or diagnosis with him.

Honesty is moral soundness: rectitude is that integrity chiefly applicable to social transactions, *sincerity is honesty of mind or intention*. The fact that patients are honest and sincere in their belief that they have physical complaints that can be rectified by injections, treatments or surgical operations does not in itself justify the performance of such procedures It is unfortunate that the carrying out of therapy by some practitioners of the healing arts, honest and sincere but not thoroughly grounded in the scientific principles of medicine and surgery, has subjected patients unnecessarily to injections for toxic conditions and to surgical removal of appendices and gallbladders and, in women, of the internal genitalia.

It is appropriate here to quote from Oliver W Holmes. "There is nothing men will not do, there is nothing they have not done to recover their health and save their lives. They have submitted to be half-drowned in water, and half-choked with gases, to be buried up to their chins in earth, to be seared with hot irons like galley-slaves, to be crimped with knives like codfish, to have needles thrust into their flesh, and bonfires kindled on their skin, to swallow all sorts of abominations, and to pay for all this, as if to be singed and scalded were a costly privilege, as if blisters were a blessing, and leeches a luxury. What more can be asked to prove their honesty and sincerity?" (*Medical Essays*, Boston, pp. 378, 379)

Patients who have a heightened threshold for suggestion may become either alarmed or highly pleased at the suggestion of a particular diagnosis. In either case, what the physician has said about the diagnosis of a certain train of symptoms may create in the patient's mind a permanent disorder or an erroneous belief about the disease or disorder from which he suffers.

may be told by the physician that his fatigue may indicate some organic disease Specialists in the diseases of the chest have emphasized the importance of fatigue in early pulmonary tuberculosis to the extent that the term fatigue is firmly associated with this disease. However, fatigue is common in low-grade infections and more especially in the psychoneuroses

It is true that organic disease may be overlooked and the patient treated for functional disease, but the reverse is more often true and frequently more disastrous.

When surgical operation is indicated for organic disease in the presence of functional disorders, explain to the patients the difference between the two and do not leave the impression that repairing the lacerated perineum, cauterizing the cervix, suspending the uterus, removing the gallbladder or the appendix, is going to restore to them a stable nervous system. The surgeon is too often pleased by the temporary relief due to the rest in bed following operation, and by the diversion of patients' minds from their troubles to their operations Unfortunately the relief thus obtained is not lasting.

As has been stated, iatrogenic and iatrotechnical disorders may occur in any topographic region or system of the body. Physicians try to prevent them. One helpful way in preventing them is to realize that the patient may be wrong in the report of what the foregoing physician has said or done.

Concluding Remarks in Regard to the Complaint. In an occasional instance it may be wise for the physician to disregard the initial complaint of the patient and to follow through chronologically each and every departure from health to the present time and then make his own conclusions how best to proceed

THE HISTORY: ANAMNESIS

In the elaboration of the complaint much time, as has been indicated in the foregoing discussion, may be necessary in obtaining the *what, when, where* and *why.* The *what* is the concept of the patient of the cause of the initiating factors of the illness, the *when* is the time sequence of the events, the *where* is the position of the patient in relation to place and person, and whether or not the patient was affected inwardly or outwardly by the environment Environment here means the surrounding conditions, influences or forces The classification of the what, when and where constitutes the *why,* and thus is the history

The history arbitrarily is divided into the present illness, the past illnesses, which may or may not pertain to the present illness, and the family or genealogic history, which likewise may or may not pertain to the present illness. A classification of the attestations of the nature and purposes of the complaint may embrace all of the arbitrary divisions of the history but usually only the present illness.

Before one begins the recording of the history, it is well briefly to relate the complaints back to the patient and ask for corrections and elaborations. If the events and complaints can be quickly verified by the patient, the first definite piece of diagnostic information is at hand, the complaints are based on organic disease If the patient heckles and makes many changes in and additions to the complaints when they are related back to him, likely the disease or disorder is of functional or nervous origin. Thenceforward the physician questions in his own mind the validity of all assertions and complaints the patient may utter

The History of the Present Illness. The complaints having been obtained, the present illness can be separated In most instances the present illness is but an elaboration in sequence of the origin and development of the complaint or complaints.

During their training, medical students commonly are admonished that in practice the physician must obtain a full and careful history in each case. A full and careful history may not be obtained in some instances on one survey of the illness. It is obtained or, rather, built up by repeated attempts often extending over days. Emphasis may change when the patient has had time to ponder the questions asked.

ries a severe social disapproval. A physician who remarks to a self-conscious patient that "you may have syphilis" may create a disorder more serious than syphilis itself. (2) False positive serologic reactions The treatment of false positive serologic reactions by antisyphilitic therapy often creates a serious iatrotechnical disorder (see False Positive Serologic Reactions, Chapter 17)

Iatrogenic heart complaints and disorders may be found to have originated from the statement of some life insurance examiner or physician to the effect that the heart shows some abnormality such as a murmur or irregularity of rhythm as revealed by the electrocardiograph; or else from the rejection of the applicant for life insurance on the score of some heart disturbance or of high blood pressure. Sometimes it is a mere assumption on the part of the applicant himself that the heart must be diseased because two or three examiners were called in to listen to it In a person of the appropriate mental composition, the slightest suggestion that the heart is not intact may be enough to start a myriad of emotional reactions, which are very difficult to subdue if the patient has a relative or friend who happens to succumb suddenly to a coronary occlusion

An individual may have forgotten, for a long time, the remark of a doctor about some minor abnormality in the heart action until there appears some symptom which calls the attention of the patient to the heart and renews the doubt that might have once existed as to its integrity The renewed interest in the action of the heart may be created by a sudden skip or a twinge of pain, or may be merely what is regarded as undue palpitation or dyspnea after some special exertion. Such disturbing symptoms are often first noticed during convalescence from an illness

In eliciting the complaints of patients it is not to be supposed that organic heart disease is found only in individuals who have stable minds and nervous systems Organic heart disease does occur in those whose mental make-up predisposes them to apprehensions and fears These patients will have a tendency to complaints explainable on the basis of organic heart disease and too there will be complaints and symptoms which cannot reasonably be ascribed to the heart disease present However, when a structural disease is itself causing severe or distressing symptoms, the neurotic symptoms, if present at all, are likely to be relatively unimportant It is in the milder forms of heart disease, with few or no real symptoms, that the complaints due to emotional reactions tend to occupy the foreground. A correct differentiation between the complaints which are the legitimate result of the existing organic disease and those which are merely the expression of the associated psychic upheaval demands skill, judgment and experience Experience and common sense dictate just what is to be expected in the way of symptoms from the type and grade of the organic lesions present in order to recognize that certain of the symptoms have no direct relation to the somatic disease

This association of organic disease with complaints of a purely neurotic nature is encountered in cardiac patients of almost all ages Older children who have rheumatic heart disease have been taught by an overanxious mother or physician that all physical effort is to be avoided They complain of what they have been taught to expect if exercise is attempted Neurotic women who have long-standing but relatively mild mitral stenosis and persons in middle life who are oppressed by the knowledge that they suffer from high blood pressure may be full of complaints given to them by a physician, the physician having diagnosed their heart disease by means of an electrocardiogram Physicians, some of them, are much too prone to regard physical overexertion as the most serious hazard to which cardiac patients are exposed, and to fail to give proper weight to the potentialities for harm that reside in violent psychic stimuli and prolonged sedentary habits

Iatrotechnical disorders and complaints often arise from the treatment of a patient for functional disorders as organic disease. The patient is submitted to unnecessary medical and surgical treatment, thereby intensifying the neurosis. Such a patient

disease cannot be overestimated Each symptom should be elicited and the time of its appearance correlated with the chronology of the other symptoms

The statements of patients with reference to the therapeutic agents used by physicians previously consulted are ordinarily untrustworthy. If such knowledge can be obtained from authoritative sources, however, it may be of considerable value. Thus certain symptoms, otherwise unaccounted for, may be explained as due to the administration of certain drugs.

The Past History. The past history includes information about the patient, the age, sex, nationality, occupation, places of residence, habits, experiences, sensations and previous diseases or injuries Such considerations embrace also the chronologic occurrence, seasonal or diurnal, of certain diseases, and the comparative infrequency of others. These incidents are first entered in outline form and later translated chronologically as the history is written for permanent record.

AGE. Anatomic structure varies with age, and physiologic processes have peculiarities which are characteristic of different periods of life. Moreover, the effects of environment, occupation, habits, the beginning and end of sexual life, and the wearing out of the organism are manifested at varying ages. Consequently there is a distinct preponderance in the frequency of certain diseases or classes of disease at special age periods. The diseases of youth are often the direct progenitors of those of old age, and the life of the individual may be a constant struggle with disease of hereditary origin or with disease that began in prenatal life

SEX. Putting aside the diseases due to differences in structure and function between men and women, there remain certain maladies which have been said to occur more frequently in one sex than in the other. These discrepancies are attributable mainly to manner of life and in women to disabilities incident to gestation Men have been said to suffer especially from diseases induced by exposure, by hard physical or mental work and worry, and by the acquirement of injurious habits. Women, more commonly than men, lead an indoor life, and many are harassed by household worries and domestic anxieties which create a special environment. In the diagnosis of disease, statements concerning differences in habits of men and women are of minimal value

RACE. The susceptibility to disease, or its opposite, immunity, possessed by certain races has caused much comment. Often the data presented favoring racial immunity or susceptibility are not convincing, for there have not always been clear definitions of the term race The terms race and nationality are not always synonymous (see Races, Chapter 16).

OCCUPATION In considering the effects of occupation in causing disease, it will be found necessary to ascertain the nature of the patient's employment, whether active or sedentary, and whether or not the work requires handling of injurious tools, or handling of toxic or irritating substances or inhaling them Hobbies, habits, and contacts with animals are details a knowledge of which may be useful. Previous occupations should be ascertained The state of health sometimes enforces the occupation

RESIDENCE. Knowledge of the place of the patient's residence may be of considerable importance, if not with regard to diagnosis, at least with regard to prophylaxis of future attacks. In the diagnosis of the fevers the fact of the patient having visited or lived in countries or localities where these diseases are prevalent may furnish a clue otherwise lacking Malaria, hookworm, fungi and rickettsial disease are examples of diseases which have at times special affinities with certain localities.

Other items embraced under the head of residence concern the effects of climate, of residence in city or country, seashore or inland; and the sanitary condition of dwellings with reference to ventilation, drainage, heating, cleanliness, water and food supply and the availability of sleeping nets for protection from insects.

HABITS The habits formed by individual persons are interwoven with age, occu-

Likewise the recorder of the history will desire to inquire about other happenings, after time has passed. He tries first of all to get all the complaints arranged according to the systems from which they originate; in generalized disease he attributes them to the body as a whole; emphasis then will usually be obvious.

The historic data having been arranged according to topography or to the system of origin, the etiology, if not already evident, is sought In obtaining data pertaining to etiology, direct interrogation is necessary. It is mandatory to reduce the number of etiologic possibilities to a minimum In making this reduction, it is well to realize that the etiology of all diseases has been categorized in the various nomenclatures of diseases into (1) diseases due to prenatal influences, (2) infections, (3) intoxications, (4) trauma or physical agents, (5) diseases secondary to circulatory disturbances, (6) disturbances of innervation or psychic control, (7) disturbances of static mechanical abnormality, (8) disorders of metabolism, growth or nutrition, (9) new growths and (10) those diseases in which structural reaction is manifest, but the cause is unknown Some hereditary and familial diseases belong in the last category.

It would be repetitious to give here in greater detail than the foregoing outline the reasons for placing any particular disease or condition of topography or system in a certain etiologic category, for that is the object of the text of this book

It is well to realize that in obtaining the history the largest drafts are made on the tact of the physician, and it is during this time that the important relationships between physician and patient are being established The physician is not a proselytizer, the right of the patient to his own religion and morals is granted Success depends to a great degree on true friendliness, on mutual confidence and, essentially, on correct mutual understanding of the spoken word

The patient may be one of the odd persons from whom it is difficult to extract more than a monosyllabic answer, or he may be so talkative that a question can be slipped in by the physician only when the patient pauses to breathe Dense ignorance may be an obstacle, so also may shame or false modesty Exaggeration of symptoms, a too common failing, must be quickly recognized and likewise the opposite, a stoic pride in making light of symptoms and disability. These and other difficulties, for example malingering, require the exercise of skill in the art of cross-examination and diplomacy

Except in the case of suspected malingering, when the answer may flatly contradict the alleged condition, leading questions are to be avoided, especially with impressionable or ignorant patients For instance, it is better to say, "Did you have any pain in the head?" than "You had pain in the head, did you not?" The first question is a simple interrogation, which may elicit a reply of "Yes" or "No" The second almost forces the answer "Yes" Care is to be taken lest the patient's story should be too narrowly limited, otherwise a knowledge of important symptoms may not be gained. It is well to expend additional time and patience and, if required, to lower questions to basic or even to depraved linguistic levels, in order to make sure that a possible vital point in the history is not missed.

An important point, with reference to early diagnosis of a host of diseases of infectious origin, is to learn of any known exposure. Another important diagnostic aid is information about fatigue of mind or body, dietetic imprudences, toxic agents, and chilling of the body or taking cold This last factor is frequently assigned by patients as a satisfactory etiologic explanation of the most diverse ailments.

A definite statement of the time of onset will generally place the disease in one of two categories, acute or chronic As a rule, acute diseases begin suddenly, whereas chronic maladies may continue over a long period before the symptoms force themselves on the attention of the patient.

The manner of onset should be accurately ascertained by separating the symptoms which initiated the attack from those which appeared at a later period. The value of a strict chronologic history of the symptoms which succeed the onset of any

ing diseases, in their prognosis or as suggestive in regard to their possible occurrence in a given case: deficiency states, myocarditis, cirrhosis of the liver, chronic pharyngitis, chronic gastritis, delirium tremens, neuritis and Korsakoff's disease.

The Family History. The family history of the patient is of much importance because of the light which may be cast by it, not only on the present illness, but also on the constitution and tendencies of the patient.

It is not always possible to obtain a complete and accurate family history. It is usually necessary to cross-examine the patient with some particularity, inquiring into the symptoms and duration of illnesses attributed to ancestors, and bearing in mind the approximate meanings of various common terms. For instance, old age is frequently assigned as a cause of death from the age of 50 years or more and is a term which has little meaning. In many instances in which childbirth is assigned as a lethal cause, death is found to be due to some other cause.

Inquiries regarding certain diseases should be made cautiously because of the possibility of arousing feelings of shame or fear. If it is apparent that shame and fear exist, it is better to ask about the symptoms without mentioning the names of suspected diseases such as syphilis, tuberculosis and cancer. A feeling of reproach to family or personal pride in acknowledgment of the existence of certain ailments may lead the patient to conceal important information.

A full statement of the family history includes the nature of the illnesses (with the age of the living) and the causes of deaths (with the age at death) which may have occurred among the patient's parents, paternal and maternal grandparents, brothers and sisters. It is requisite at times to ascertain similar facts with reference to aunts, uncles and cousins. It should be borne in mind that transmissible tendencies may pass over one generation and may be sex-linked Also it is just as important to know, and to inform a young couple whose first child is born defective, that malformations are often sporadic. In an isolated case of a congenitally defective child in a known normal genealogic history there is no reason to suspect that subsequent children will be abnormal Occasionally, however, contributing factors can be discovered if the basic information is at hand. In general, the study of the causes of congenital malformation has yielded definite knowledge concerning some causative factors It may be pointed out that German measles (rubella), toxoplasmosis and irradiation are known causes of congenital malformations.

COMMENTS

While discussing the complaint and the history, the physician forms a conception of the mental characteristics of the patient, in health and as modified by disease. As a rule, the more highly trained the mind, by private study or at college or in business, and the more elaborate and complex the social environment, the greater is the necessity for an appreciation of the personal traits of the individual. Influences which produce no apparent effect on some laborers, toughened by hard life, will cause profound perturbation in the somewhat hyperesthetic person, man or woman, whose nervous system is in a state of tension from the demands of family, society, art, literature or religion

If necessary, information may be obtained from friends or relatives concerning the mental traits of the patient in health, but such information should not be accepted without proper consideration of its source. Inquire especially as to the existence of extreme susceptibility to pain and of exaggeration in the manner of expression; as to whether the patient is or is not easily elated or depressed, or given to undue solicitude about personal health, of himself and of others, and other points which may be serviceable in estimating the value of the statements made by the patient or the present deviation from the normal mental and physical health. Such inquiries should be made with circumspection and tact in order to avoid misconception of motives

pation and residence. The possible existence of addiction to alcohol, opium, cocaine or other drugs is always present. Diet; the use of tea, coffee and tobacco, clothing, sleep and exercise are largely governed by the social condition and environment Both men and women should be interrogated as to the amount and strength of tea and coffee taken daily. The tea-and-cake habit is mainly found among women. The examiner should ascertain also the kind and amount of alcoholic beverages taken and the time of taking; that is, whether before, during or between meals; and how much tobacco is used, of what kind, and in what manner (with reference to nasopharyngeal catarrh, nervousness and cardiac neuroses).

The experiences of an individual depend on many factors, among which are personality, type, and physical stamina The experiences and sensations are recorded only if pertinent to the present illness

Previous Diseases or Injuries. A knowledge of prior illnesses and injuries is of value, provided that their date, nature and severity can be ascertained, for three reasons.

1. An attack of any of certain *diseases renders subsequent attacks of that disease probable* Among such diseases are angina pectoris, apoplexy, appendicitis, asthma, pneumonia, bronchitis, tonsillitis, colics (gallbladder and renal), convulsions (infantile or epileptic), malaria, gout, migraine and neuralgias

2 With many of the epidemic fevers of bacterial, viral and rickettsial origin, a previous attack may negative its subsequent occurrence

3. A *history of the previous existence of certain diseases or injuries may throw light on present conditions* which stand in the relation of sequelae to the primary ailments Examples of these diseases are syphilis, gonorrhea, scarlet fever, rheumatism and chorea, and septic or suppurating foci, leading to subsequent embolic or general inflammations of heart, lungs, liver, pleura, bones, or peritoneum, any or all of them

A history of a fall or other injury may be of some value in arriving at a diagnosis, for instance of a protruded intervertebral disk, jacksonian epilepsy or sympathetic ophthalmia A previous surgical operation may point to the possibility of a recurrence of the condition which required operative intervention

There is little of diagnostic value to be gained from the varying statistics of the *seasonal prevalence of disease* in the United States, beyond the broad statement that diarrheal diseases predominate during the summer months, and poliomyelitis in late summer, whereas pulmonary disorders and rheumatic affections are most prevalent in the winter and early spring Zymotic diseases occur in largest number during the cold season, but this is to be explained rather by the opening of the schools and the closing of house windows than by the effect of season in itself

It may be mentioned here that certain diseases either begin or show an *exacerbation of symptoms at special diurnal periods.* Bronchial asthma is likely to make its onset or to intensify in severity in the early morning hours; spasmodic croup, as well as diphtheritic stenosis of the larynx, between 10 P M and 12 P.M The suffering from painful diseases is usually worse at night, and in febrile disorders the temperature generally reaches its highest point between 7 P M and 8 P M. The paroxysms of whooping cough are more frequent and severe at night than at other periods The pain due to diseases of the bones, joints and peripheral nerves presents a nocturnal aggravation Pain of rheumatoid arthritis is likely to be worse when the patient arises in the morning than at other times

It is well to remember that some ailments present a more or less regular *periodicity of recurrence.* Among these are neuralgias, migraine, epilepsy, periodic paralysis, relapsing fever, malarial infections, ulcerative endocarditis, paroxysmal hemoglobinuria, pyelonephritis, bronchial asthma and menstrual disorders.

A history of *alcoholism* is important as explanatory of the presence of the follow-

and the charge of making imputations uncomplimentary to the patient. The physician in private practice has favorable opportunity to please and help, because in consulting him the patient has exercised choice in seeking personal advice. The physician in institutional practice conducted by a group or a governmental agency has more difficulty because the patient may not have had a choice of physician.

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3

EXAMINATION

For the general examination the patient is fully undressed of the usual clothing An appropriate dress for the examination is a cape about the shoulders and a sheet around the waist. Many other suitable garments have been devised and all are satisfactory

Manner and Dress. The physician begins to observe the manner and dress of each of his patients as soon as acquaintance is made.

The manner of a patient pertains to the method of performing or executing the ordinary social acts over which custom presides Each individual has a peculiar mode of performing these acts, depending on the training which has been molded by the environment to which he is accustomed. This definition of manner assumes that the individual under observation is reasonably free from physical discomforts and mental stresses. The psychic and physical stresses of illness often change the manners of both men and women For instance, an individual who is suffering from hysteria under normal conditions of life may under the adversities of an additional illness to himself or to a member of his family, behave in a stable and admirable manner An individual of good manners when in health may express a bad manner under the stress of illness and pain in himself or in members of his family.

Modern dress is no longer an expression of status or determinate function There remains a well-developed sense of decorating the body with clothing and accessories such as jewelry and furs. In individual instances it is frequently difficult to differentiate between clothing and ornament, this is especially true of the headwear of women. Cultists with distinctive mental warping may dress foolishly, solely for the purpose of exhibition, justifying such dress by reference to the Scriptures, as, "If I may touch but his clothes, I shall be whole" (*Mark V*).

Although clothing no longer is a symbol of class distinction, it may have diagnostic implication in the individual or in groups of individuals. The most significant implication is related to the sexual representations or aspirations of the female During the last 200 years women's dress has changed constantly and alternately in an endeavor to conceal or to reveal the back, breasts, shoulders, arms, legs and thighs During the period of a particular vogue all women, good, bad and indifferent, will and should conform to the fashion The physician is not interested in fashion or in those who conform to fashion, but in those who do not conform. Of definite interest to the diagnostician are two small groups, namely, those who become conspicuous by showing more of the thighs than fashion permits, and those non-conformists who show none of the thighs despite fashion Those who show too many charms are likely to be involved in sexual and marital intrigue or think they might like to be. [illegible] social diseases as well as being [illegible] physically beautiful and deli- [illegible] Those who show none of their [illegible] fected by all sorts of abnormal ergasias.

Of the accessory articles of dress, tinted spectacles, when worn because of "weak eyes" if there is no disease of the eyes, indicate that the wearer admits poor health Excessive and gaudy jewelry, even expensive ornaments of excellent workmanship,

often adorns selfish persons. Perfumes, in profusion, except among Latins, may indicate the absence of the regular use of soap. Distinctive, highly aromatic perfumes are often used by those afflicted with homosexual and heterosexual practices.

In the evaluation of patients with regard to their clothes, the examiner has in mind that with the majority the influence of social customs prevails, as expressed in the Arabian proverb, "Eat what you may, but dress as others do."

An occasional hint may be derived from care of the dress. Omission to use fastenings which may be needed for common decency, the coat or trousers buttoned with the wrong buttons, or a vest soiled with droppings of food may indicate the mental enfeeblement due to psychosis or chronic alcoholism, or due to the physical disability resulting from arthritis or paralysis. Clothing wet and of ammoniacal odor is observed in cases of incontinence of urine and cystitis; when urine dries, it may leave a white deposit on the clothing. A patient may be so crowded and bulging in his clothes as to suggest a recent rapid increase of bulk from obesity or general dropsy. The shoes may be left partly or entirely unfastened from forgetfulness, gout, rheumatism or edema; or slit for similar reasons, or because of corns, bunions or injury; or worn more on one side, or in front, or at the heel, because of paralysis, deformity or disease of the joints

A great deal may be gleaned from the behavior of an individual when asked to disrobe for the examination. A proper amount of timidity at having to undress for an examination is expected of both sexes. Extremes of timidity may interfere with or prevent a satisfactory examination. If the examination is rendered unsatisfactory or impossible, this should be made clear to the patient. Insistence and persistence never accomplish anything Patience on the part of the examiner, with full explanation of the reason for an examination, usually gains the desired results.

During the examination the examiner extends his knowledge and attempts to confirm those things which have been learned from the complaint and the history. He employs his own functions of knowing, combined with his feelings and his strivings, to learn and to demonstrate wherein the trouble lies. He looks (inspection), he feels (palpation), he listens (auscultation), to determine the condition of the tissues. These primary methods of sight, touch and hearing have many applications and combinations, the simplest of which is percussion, a combination of touch and hearing Sight, touch and hearing are the primary methods of examination of the patient It should be realized that native capacity for employing the senses varies with each person. Only a few have the natural capacity of Laennec, Trousseau and Flint, and it is these few who do not argue about the relative merits of palpation, auscultation and percussion versus roentgenologic examination or any other way of objectively demonstrating derangement of tissue by trauma or disease. These few physicians and surgeons who have natural ability do not argue; they are happy to find for themselves the source of disease, or they cheerfully accept the help that anyone or any appliance or other means can give them. Any person endowed with an average degree of the sense perceptions and intelligence can learn the technic of studying and examining patients A lack of acuity of one of these senses may be overcome by constant effort, practice and development of the other senses. For all, it must be known that at least three out of four illnesses are diagnosed and treated from the diagnostic data obtained by the physician from the use of his senses and his knowledge of disease

Theory and Practice of Inspection. Inspection, which is begun with the first sight of the patient, is the most valuable method of examination During the taking of the history the sex, approximate age, race, posture, facial expression, nutrition, color of skin, eyes and hair, and many other details are observed. During any part of the taking of a history and the performance of an examination the examiner requests, "Let me see you do it," or "Show me where the pain originates and where it goes."

The light, preferably daylight when feasible, as a rule should fall directly on the surface to be examined Changes in direction from which the light comes, controlled by moving either the patient or the source of the light so as to permit the rays to fall obliquely across the surface to be examined, are often of value by production of shadows and may accord emphasis of much use in detecting small pulsations or abnormalities of shape and movement.

Theory and Practice of Palpation. Palpation, the use of the tactile sense of the hand and fingers, is an indispensable means of obtaining information in all manners and means of diagnosis. The remarkable extent to which the educated touch may be developed is exemplified in many physicians

In the practice of palpation care should be taken to keep the nails short. The hands should always be warmed before touching the patient. All rough or abrupt pressure is avoided The hand at first should be laid flat on the part, later the fingers and their tips may be employed to determine and localize more accurately any discoverable abnormality When palpating deep-seated organs, or when there is a large amount of overlying fat or fluid, the palpating hand may be usefully reinforced by pressing on it with the other, thus sparing the palpating hand much muscular exertion and leaving unimpaired its power of tactile appreciation

When palpating, the points to be determined with reference to the part or organ are temperature, shape, size, measured (stated in metric terms), consistency; movability, with or not with respiration, tenderness, superficial or deep-seated; fluctuation, the undulation of an enclosed fluid produced by the pressure of the fingers, and appreciated by another finger placed on the opposite side of the enclosing cavity, fremitus, pulsations, thrills or vibrations originating in the heart or blood vessels

The synchronous use of the methods of inspection and palpation is to be encouraged When these are used separately, always look before feeling—and feel before listening.

Theory and Practice of Auscultation. Auscultation may be performed by direct application of the ear to the body or it may be aided by use of the stethoscope Auscultation may be combined with inspection and palpation (see Diseases of the Respiratory System, Chapter 9)

Directions and Topography. In the examination of patients directional terms for description of findings are employed constantly, and it therefore is important to use the proper terms that do not permit confusion. Such terms as *front* and *back*, *top* and *bottom*, are not desirable For the trunk, *dorsal* and *ventral*, *cranial* and *caudal*, are the proper directional terms, but are not generally employed, *anterior* and *posterior*, *upper* and *lower*, *apex* and *base*, are the terms in use, though they may admit of confusion *Dorsal* and *ventral* are permissible, but not wholly admirable, terms applicable to the inferior extremity and the upper arm as well, for these aspects are constant in orientation with the trunk. The terms *superior* and *inferior* are so firmly entrenched in diagnostic descriptions, particularly in connection with aspects of the vertebrae and as names of structures (as M. serratus posterior superior), that they cannot be abandoned The term *superior extremity* is diagnostic and almost always is used instead of the more correct designation, *pectoral extremity* The meaning of *anterior* and *posterior* when applied to aspects of the ankle is likewise clear, but when applied to the wrist, it is not clear, for the wrist is reversed in pronation and supination In designating aspects of the wrist, *dorsal* and *volar* (*or palmar*) are the proper terms

Cranial and *caudal*, though technically proper terms for the aspects of the head, are clumsy. The head of man is oriented on the same axis as that of quadrupeds, and *anterior* and *posterior*, *superior* and *inferior*, are permissible terms. *Lateral* and *medial* directions in the upper arm and in the inferior extremity may be used, although *fibular* and *tibial* in referring to sides of the lower leg and the foot are prefer-

able. *Lateral* and *medial* directions are objectionable for forearm and hand because it is not known whether the natural or the anatomic positions are meant. For these, *radial* and *ulnar* directions are correct.

Directional terms of a general nature, in antithetic pairs, are as follows (based on Howell's *Gross Anatomy*, D. Appleton-Century Co, 1939):

Anterior and *Posterior*. front and back, respectively; properly used for the head only, but permissible at times, because of established usage, for the trunk. The proper corresponding terms, except for the head, are the following:

Dorsal and *Ventral:* The term dorsal indicates the back, the entire back or upper side of an animal when the ventral surface is down. Dorsal is incorrectly used to designate a particular segment of the back, for instance that of the thorax. Likewise ventral is not for the front of the thorax. The thoracic vertebrae are often incorrectly designated dorsal vertebrae. Since vertebrae are identified according to the region of the back to which they belong, for instance as cervical, thoracic, lumbar, sacral and coccygeal it is incorrect to designate any of them as dorsal vertebrae. They are thoracic vertebrae In instances of increases over the usual number of vertebrae in a particular region, the extra vertebra is designated by addition to the usual number for that region, for instance a sixth lumbar vertebra. The dorsal aspect of the limbs, both upper and lower, is the part covered by the dorsal or extensor musculature. The dorsal aspect of the arm is the back of the upper arm, back of hand and wrist and the corresponding aspect of the forearm. The dorsal aspect of the inferior extremity is the front of the thigh, leg and upper part of the foot.

Dorsal and *Volar* (or *Palmar*): the proper terms for back and palm, respectively, of hand, and corresponding aspects of forearm.

Dorsal and *Plantar*. the proper terms for upper aspect and sole respectively, of the foot.

Superior and *Inferior:* permissible but less desirable (except for head) alternatives for cranial and caudal.

Cranial and *Caudal:* the proper terms for the indicated directions in the trunk.

Superficial and *Deep:* superficial is nearer the surface (from any aspect), as opposed to deep.

Medial and *Lateral:* medial is toward the median plane, and lateral is toward the side.

Peripheral and *Central:* peripheral, toward the periphery, central, away from the periphery. Used mostly in connection with the nerves.

Proximal and *Distal:* proximal, toward the median plane; distal, away from the center. Used mostly in connection with the extremities and the alimentary tract. In the alimentary tract proximal is employed to designate nearest to the mouth or to the beginning of the segment, irrespective of topographic situation. For instance, *proximal jejunum* indicates that part nearest to the stomach or the mouth even in the presence of situs inversus viscerum In the alimentary tract, particularly the intestines, *distal* indicates away from a designated point. It is used in opposition to proximal. Common use of these terms is in connection with artificial stomas; for instance, proximal stoma, the one which discharges the intestinal dejecta. *Distal stoma* designates the direction in which the intestinal contents would or do flow away from the stoma

External and *Internal* used chiefly to indicate respective surfaces of hollow organs, or of the body as a whole.

Radial and *Ulnar* the proper terms for denoting the sides of forearm, wrist, and hand; toward the radius and toward the ulna, respectively

Tibial and *Fibular* the proper terms for denoting the sides of the lower leg, ankle, and foot, toward the tibia or toward the fibula, respectively.

The following terms in frequent use might prove confusing unless explained:

Mediad: toward the median plane.

Medius: middle; between dorsal and ventral or between external and internal

Intermedius: between medial and lateral.

Transversus: transverse to a particular part of the body.

Transversalis: transverse to the body axis.

Transversarius. relating to some structure which is transverse (as Mm. intertransversarii, the muscles between transverse processes).

As the body is three dimensional, so there are three planes of the body:

Sagittal Plane: the dorsoventral longitudinal plane; through or parallel to the sagittal suture.

Coronal or *Frontal Plane:* the longitudinal plane, from side to side, at a right angle to the sagittal suture; through or parallel to the coronal suture.

Transverse Plane. the horizontal plane, at any level, at right angles to both sagittal and coronal planes.

Anatomic Regions. The primary regions of the body, as discussed here, comprise *head* (caput), *neck* (collum), *back*, and *superior* and *inferior extremities*. Each of these is customarily divided into secondary surface regions. The boundaries of some of these are not always to be determined with accuracy by one inexperienced in anatomy, for the reason that their extent usually depends on some subsurface feature Anyone interested will find by reference to the *Basle Anatomical Nomenclature* (B N A) list of regions, that many of the secondary regions (as parietal, frontal, deltoid, posterior femoral and the like) are self-apparent, and that some other terms are of but little use in diagnosis

In this text each of these regions is described in association with the topography and topographic diagnosis when that particular region is being considered. Generally the requirements of the *Basle Anatomical Nomenclature* are at least respected and partially fulfilled.

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4

TOPOGRAPHY AND REGIONAL DIAGNOSIS OF DISEASES OF THE HEAD AND ORGANS OF SPECIAL SENSES

The general practitioner and the internist are not expected to make specialized examinations and diagnoses or to carry on specialized treatment. However, they are required to have sufficient knowledge of diseases described and diagnosed by the specialist to discuss intelligently with the patient the diagnosis and treatment which the specialist suggests in the individual case. In the discussion that follows, it is hoped that there is information which may be of some help to the physician in his fulfillment of his obligations to the patient.

The head varies in shape and size according to race, sex and age. As a rule, the head of a man is larger than that of a woman. The head tends to change shape and increase in size with age. If the head enlarges out of proportion to the rest of the body, the condition is designated as *macrocephalia*. If the enlargement tends to produce mainly a broad head, the condition is designated as *brachycephalia* If the enlargement tends to produce a conical-shaped head, the condition may be designated as *oxycephalia*. If the head is unusually long from front to back, the condition is known as *dolichocephalism* If the head is unusually narrow, the condition is designated as *stenocephalia*, if the head is unusually small, as *microcephalia*, and if the head is generally distorted and of abnormal shape, it may be designated as *plagiocephalism*

In many men past middle age an increasing prominence of the supra-orbital ridges develops, with the result that the eyebrows seem to overhang the eyes more and more and the countenance looks different from what it did 10 or 20 years earlier. This enlargement is due to or is associated with enlargement of the air cells of the frontal sinuses and is not pathologic However, if this enlargement of the forehead is excessive, it must be distinguished from acromegalia and from another condition, of no clinical significance, formerly designated leontiasis. Leontiasis may or may not be associated with a thickening of the frontal bone which is known as benign frontal exostosis, this too is of no clinical significance. Often a patient who has enlargement of the forehead seeks medical advice with the complaint that he has noticed that the size of his face is increasing; such a patient nowadays wonders whether or not he has disease of the pituitary gland. The condition can be distinguished from acromegalia in that rarely in acromegalia is the frontal bone alone affected, and more often the affection of the forehead is much slighter than the increase in the size of the lower jaw and the phalanges of the hands and feet Tumors of the frontal bones almost always cause an asymmetric enlargement

Changes of Shape and Contour of the Head in Disease. In certain diseases characteristic changes in the size and contour of the head and face are of diagnostic importance

In *hydrocephalus* the head is abnormally large and usually globular, sometimes pyramidal, in shape Hydrocephalus is most frequently observed in infants and children. An abnormal increase in the measurement of the head is the principal symptom by which chronic hydrocephalus can be recognized Aside from the en-

largement the most characteristic feature is the prominence of the forehead at the root of the nose The rachitic head may resemble a hydrocephalic head. Many children recover from mild degrees of hydrocephalus. The only evidence of it left in adulthood is an increase in the size of the forehead which gives the appearance of a rather large dome-shaped head

Heads deformed by *rickets* and changes of the head produced by sporadic *cretinism* or *myxedema* are described in appropriate places in subsequent chapters.

If the face presents an appearance as if it were composed of lateral halves from two different individuals, with the vertical line of junction sharply defined, and if the hair of the smaller side is thin or absent, the eye sunken and the skin altered in appearance, it is probably an instance of facial *hemiatrophy*

If both sides of the face appear normal but one is much the larger, the condition known as *congenital hemihypertrophy* should be suspected. Along with congenital hypertrophy, hemangioma of the skin over the affected regions often is present. Since congenital hemihypertrophy often involves one half of the body, confirmation of congenital hemihypertrophy should be sought by making comparative measurements of the arms and legs The arm and the leg which are hypertrophied may be on the same side as the hypertrophied half of the face or they may be on the opposite side

Facial asymmetry may exist also with congenital torticollis or wryneck. If the cranium is enlarged and globular, and the malar prominences are marked and the orbital rims massive, the presence of hyperostosis of the cranium should be suspected

The tuberous growth of *leprosy* occurring on the face, together with the resulting ulceration and cicatrization, slowly changes the shape and contour of the countenance, which assumes the so-called leonine aspect or facies leonina

Tower-shaped skulls are rather characteristic of some of the congenital anemias (see Hemic Diseases, Chapter 11)

Abnormal Movements of the Head. *Nodding spasm* is a rhythmic nodding movement of the head In children this movement may be a form of habit spasm or of epilepsy In cases of epilepsy or convulsive disorders nodding spasm is accompanied by a momentary loss of consciousness. It may occur in hysteria, either alone or as a part of the so-called *hysterical chorea*

Pulsating shaking of the head, which occasionally is seen in the aged, is not necessarily evidence of senility or arteriosclerosis. It seems at times to have a *hereditary factor It is often found in postencephalitis* or Parkinson's syndrome.

Spasmodic torticollis is a spasmodic jerking of the head which recurs every few minutes. In the chronic form of the disorder the head is brought toward one shoulder, which may be simultaneously jerked upward to meet the head at the same time that the face is rotated to the opposite side and the chin is raised. In chorea, as contrasted with spasmodic torticollis, the movements of the head are extremely irregular and bizarre, and the facial muscles are affected before those of the neck. Torticollis is often a form of conversion hysteria

Inability or disinclination to move the head, especially if the patient is prone to support it by hand, may be due to disease of the cervical vertebrae. If this manifestation is associated with dysphagia, it points to disease of the articulation between the atlas and the occiput.

Retraction of the head of a bedridden patient—that is, a drawing back and *fixation* of the head by contraction of the posterior cervical muscles so that the occiput bores into the pillow—is a symptom in all forms of cerebral and cerebrospinal meningitis, particularly when the disease is affecting the basal meninges It is seen in tetanus and in strychnine poisoning as a part of the general tonic spasm.

Other causes of abnormal fixity of the head are occipital cervical myalgia and cervical arthritis, swollen and painful cervical lymph nodes, sprain of the cervical muscles or other traumatism of the neck, postpharyngeal abscesses, congenital and

spasmodic torticollis, and contracted cicatrices, especially extensive scarring from burns

THE SCALP

The *skin* of the scalp is the thickest in the body, although not so dense as that of the heel. Besides the hair follicles, the scalp contains abundant sweat and sebaceous glands and blood vessels, which are associated with the hair follicles

The *hair* of the scalp is to a very slight extent an index to the general robustness and vigor of the individual Thick coarse hair is at times associated with strength of constitution, and scanty fine-textured hair with a delicate habit of body, but there are many instances in which this is not the case. There is some diagnostic value in an observation of the color and scantiness of the hair (see page 1197).

Loss of Hair Color. Graying of the hair, the physiologic loss of the pigment of the hair, begins in the average individual at 40 to 45 years of age and slowly increases as the years pass. Early grayness is not always a sign of premature old age and is not necessarily associated with degenerative arterial changes Gray hair is compatible with good health and otherwise normal tissues. The loss of color is frequently dependent on a hereditary factor.

When chronic poisoning is suspected, if it is apparent that the hair is dyed—and dyeing usually is apparent—it may be an important clue in the diagnosis (see Hair Dyeing, Chapter 19).

Alopecia (Acomia, Calvities, Baldness) The etiology of alopecia is not often obvious Congenital baldness (alopecia adnata) is rare. This is usually associated with defective teeth and nails. These two conditions are of little practical importance diagnostically.

Premature Alopecia. This is an exceedingly common condition, especially in men It is endocrine in origin; eunuchs are never bald. It is not attributable to modern civilization or to the wearing of tight hats It is familial in origin and common to all races of men

Premature alopecia begins at about the age of 20 years and is often completed by the age of 30 years, only a rim of hair being left at the back and sides. Cases, however, do occur in which the loss of hair is more gradual and, even on the vertex, may never become complete The scalp may be obviously seborrheic, or covered with dandruff, which undoubtedly aggravates the condition, or it may look normal

A corresponding type of alopecia occurs in women, but has several points of difference from that seen in men It is more general and is not limited to the vertex, is not so nearly complete, and is more regularly accompanied by seborrhea of the scalp

Alopecia Without Scarring. The etiology in alopecia without scarring is unknown A disturbance in innervation or psychic control is possible In susceptible persons a shock may precipitate an attack, during World War II attacks occurred in three or four weeks after the patients had been torpedoed or bombed. Reflex irritation from neuralgia, a carious tooth, septic sore throat or similar condition has been blamed, but these are not valid causes The patients, even those who have alopecia totalis, are usually in excellent health.

There are several varieties of alopecia without scarring, for instance, alopecia areata, trichorrhexis nodosa and trichotillomania

Alopecia Areata. This common condition is characterized by circular areas of baldness. It is not related to the color of the hair, and it affects men and women about equally In Anderson's experience there was a difference in the position of the primary patch between the sexes. in men it was 60 per cent occipital, 25 per cent frontovertical, in women it was 27 per cent occipital, 56 per cent frontovertical A positive family history was present in 19 per cent, but it is doubtful that this indicates

a familial tendency. Other members of the family were affected at the same time in 6 per cent of cases Vitiligo was present in 4 per cent of cases.

The affected hairs show thinning toward the roots and are easily removed with brush and comb. They may also break off a few millimeters above the skin surface.

Alopecia areata is a relapsing disease, beginning in childhood but more severe between 20 and 29 years of age The hair slowly returns to the bald spots, though it may be delayed for months and may grow back white and remain white. When the disease steadily progresses until all hair all over the body is lost, the alopecia usually is permanent Another resistant form of the disease is that in which the scalp margin is involved in a patchy fashion These patches may coalesce to form a band, giving a wiglike appearance to the rest of the hair.

Nail changes are common in extensive alopecia. When the nails are affected, the changes are usually in the form of rows of tiny pits, as is sometimes observed in psoriasis These pits often are unnoticed by the patient and are found only on routine examination Nails of both the hands and the feet may be affected

Alopecia areata is differentiated from ringworm by the absence of scaliness of the scalp and of fungus in the hairs. Cicatricial alopecia offers no difficulty. Furunculosis is eliminated by the fact that the scar of the original lesion has a center of a red dot

Prognosis is good in ordinary cases for patients less than 40 years of age When there is involvement away from the scalp, for example of eyebrows and the bearded areas and around the edges of the scalp, the lesions are stubborn and persistent Recovery is slow also in cases in which scattered white hairs are present on the bald patches Chronicity is universally a bad omen Alopecia totalis is to be feared in all cases in which the disease lasts more than 18 months.

TOXIC ALOPECIA There are many toxic agents, including roentgen rays and radium, that cause a fall of hair After prolonged fevers the hair may fall Falling hair results from a similar cause during the secondary stage of syphilis (moth-eaten scalp) and after pregnancy After gestation the onset may be sudden and the fall severe In all toxic alopecias an important diagnostic point is that the hair behind the ears can easily be pulled out

TRICHORRHEXIS NODOSA This condition is due to too frequent use of too strong soaps and excessive friction, as may result from a habit of rubbing the hair. The hairs show white nodes which, on microscopic examination, are seen to consist of a splitting of the hair structure so that it has the appearance of having the end worn off

TRICHOTILLOMANIA Trichotillomania is a habit comparable to nail biting Hairs are consciously or unconsciously pulled out The irritation of pediculosis may start the habit An area, or areas, of normal scalp dotted with normal hairs of varying length and a surprising amount of alopecia are the result. The diagnosis requires roentgenoscopic examination of the stomach in search for the possible presence of trichobezoar (hairball)

Alopecia With Scarring. The causes of alopecia with scarring comprise all the etiologic agents producing scarring, such as roentgen rays, radium, burns and infections, such as favus, kerion of ringworm, or lupus erythematosus. The primary cause is usually recognizable The atrophy following the use of roentgen rays or radium is a factitial dermatitis, the scars of burns are deep and contracted; favus has a long history of gradual spread and may still show marginal activity; kerion scars are circular or are combinations of circles; lupus erythematosus may show activity or scarring over the bridge of the nose and medial sides of the cheeks.

Tumors. The scalp contains an abundant blood supply and consequently telangiectasis and venous and cirsoid aneurysms are frequent (see page 316).

There are a number of tumors of the scalp of congenital origin Cephalocele, a protrusion of part of the cranial contents, may be of congenital or of acquired origin.

The cephalocele occurs in the occipital and sincipital regions, either above or below the tentorium. An *encephalocele* is a hernia of brain matter and is covered with the arachnoid; it protrudes through a congenital or traumatic opening in the skull. A *meningocele* is a cystic mass, a protrusion of the meninges, covered by pia mater. A *hydrencephalocele* is a protrusion of a lateral ventricle or of the fourth ventricle covered by brain tissue and the arachnoid.

Dermoid tumors, which consist of occluded ectoderm, occur in the median line of the head and face. They often appear over the anterior fontanel and the external occipital protuberance. Often a thin pedicle attaches the tumor to the dura mater.

Cysts. Sebaceous, epidermoid, inclusion dermoid, and mucous cysts occur about the head and neck.

Cystic skin tumors whose contents consist of keratin are keratomas, and those which are of acquired origin and which contain sebaceous material are sebaceous cysts. Inclusion dermoids are congenital cysts developing along the embryonic lines of fusion and containing hair follicles, sweat glands and sebaceous glands in their walls. Epidermoids are similar in nature to dermoid cysts with the exception that their linings possess no dermal structures.

The wens or sebaceous cysts usually occur in the scalp, and in the lobe and on the posterior surface of the ear. The common tumor of the adult scalp is the sebaceous cyst, which sometimes becomes calcified. Such tumors are usually multiple and are rounded, firm, and though freely movable are invariably attached to the skin at one point, a feature which often distinguishes them from dermoid and epidermoid cysts In the skin overlying many keratomas and sebaceous cysts, there is visible an enlarged pore from which cheesy material can be expressed on manipulation of the growth. There is a wide degree of variability in the dimensions of these tumors; some are scarcely palpable nodules, while others attain a diameter of several centimeters

Keratomas and sebaceous cysts, ordinarily symptomless, are frequently the site of an acute inflammatory process in which the tumor becomes excessively tender and painful and objectively manifests a sudden increase in size When acutely infected, the cyst resembles an acute abscess and exhibits all of the general and local symptoms which attend such a process After an acute infection subsides, a keratoma or sebaceous cyst may resume its normal proportions and appearance. In an occasional case the infection completely destroys the epithelial lining and with subsequent healing the entire cavity of the growth is obliterated. Often an acute infection in one of these tumors becomes chronic, with the result that purulent material is continually discharged externally through a sinus, producing excoriation of the surrounding skin Occasionally one of these cysts becomes chronically infected and then is surrounded by dense fibrocicatricial tissue which may completely mask the true nature of the lesion.

THE FACE

The face embraces the anterior part of the head The bony framework of the face is made up of some of the bones of the skull as well as those of the face proper Deformities and disfigurements of the face which result from injuries or disease or both assume a greater importance to the victims than comparable troubles would elsewhere, for many persons feel that their face is their fortune.

The right and left halves of the face differ from each other and present varying degrees of asymmetry. This facial asymmetry seems to be present in all races In the right half of the face the features are said to be more characteristic of the individual and are more conspicuous than in the left The right eye is more prominent than the left eye, a fact which may be related to right-handedness In the left half of the face the individual features recede.

Malformations. The relatively frequent occurrence of malformations of the face is explained by the complexity of the developmental processes in this region

nerve supply to a portion of the skin. Eating or drinking is accompanied by excessive perspiration in the area in which the nerve supply has been impaired. Langenskiold offered what he believed to be a satisfactory explanation of this distressing symptom, the preganglionic sympathetic fibers governing sweating had been destroyed, thus, according to Cannon's law, the postganglionic cholinergic fibers were rendered hyperexcitable, and during mastication acetycholine elaborated in the parotid gland "diffundated" to the nerve endings in the skin and produced sweating Gustatory asymmetric hyperhidrosis may occur below the neck as described by Mellinkoff and Mellinkoff

THE MUSCLES OF THE FACE

Facial Spasms. Spasmodic contraction of the facial muscles may be tonic, that is, continuous, or clonic, that is, intermittent. It may be unilateral or bilateral and may involve one or all of the muscles which are innervated by the facial nerve In order to form an opinion of the cause of spasmodic affections of the face, it is advisable to take into consideration the age and sex of the patient and to ascertain the presence or absence of disease of the eyes, teeth and skin In some cases the facial symptoms constitute a significant part of a disease of the central nervous system.

The diseases or conditions which may be indicated by facial spasm are mimic spasm, convulsive tic, blepharospasm, nictitating spasm, exophthalmic goiter, chorea, epilepsy, tetanus, meningitis, hysteria, spasm following paralysis, irritation at the root of the facial nerve and, finally, lesions of the cortical center of the facial nerve

Mimic spasm is usually bilateral and ordinarily does not begin until adult age A more or less constant twitching of one side of the face, with partial closing of the eye, occurring in an adult, is a mimic spasm

Habit spasm usually occurs in neurotic children. Characteristically, during the spasm there is a sudden wink of the eye or a rapid drawing of the mouth to one side or a sniff occurring at irregular intervals and greatly intensified in severity by emotional causes

Convulsive tic ordinarily is a hereditary affair occurring in neurotic children. The tic is irregular movement of the facial muscles and frequently those of the arms, and sometimes is accompanied with an explosive ejaculatory utterance of profane or obscene words, or this tic may consist of involuntary repetition of a word or the mimicking of an action

FACIAL PAIN

Infections of the sinuses and the antrums cause facial pain Dental neuritis, particularly when it occurs in senile patients, is troublesome and unfortunately is not readily relieved Often improvement of the general health of the patient by appropriate dietary regimens ameliorates the complaint The *localized dental neuritis* that follows procaine block injections is due to the excessive amount of procaine injected into the immediate vicinity of the nerve The symptoms of paresthesia usually disappear. Postherpetic *ophthalmic neuralgia* is persistent, and its course is not affected by operative procedures. Snake venom may help

The neuralgias are common causes of pain in the face In *glossopharyngeal neuralgia* the pains are projected along the distribution of the ninth cranial nerve. The trigger zone is situated in the tonsillar fossa, and the darting pains are projected toward the ear, usually terminating in the tympanum The pains are precipitated by yawning, swallowing and talking, but not by rubbing the face. The pains resemble those of trigeminal neuralgia in their occurrence, duration, repetition and character, but they differ from those of trigeminal neuralgia in their distribution. In glossopharyngeal neuralgia it will be observed that cocainization of the pharynx will result

in temporary cessation of all attacks, but cocainization of the pharynx will not alter the paroxysms when they are due to trigeminal neuralgia.

Sphenopalatine neuralgia is characterized by boring pain situated in the superior maxillary region. It is most pronounced under the malar bone, and at times extends into the gums of the superior maxilla, the hard palate and downward into the neck. This pain differs from that of trigeminal neuralgia in that it is more or less constant; it is not paroxysmal and is moderately severe, but it is not sufficiently severe to incapacitate the patient unless there is an accompanying neurosis Neither deep injection of alcohol into the branches of the trigeminal nerve nor division of the sensory root affords relief in the treatment of this type of neuralgia.

The trigeminus nerve (trifacial) arises in the medulla oblongata along the floor of the fourth ventricle and supplies motor fibers to the masseters, pterygoid, and the temporal muscles and muscles of the tongue. It furnishes the sensory fibers to the skin of the face (Fig. 4-1) and to the tongue, teeth and the corneae The three divisions of the nerve are designated the ophthalmic, the maxillary and the mandibular.

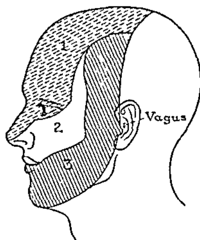


Fig 4-1. Areas within which sensory disturbances and pain may occur in diseases of the trigeminal (trifacial) or fifth cranial nerve 1, ophthalmic division, 2, maxillary division, 3, mandibular division.

Local lesions of the nerve rarely cause severe pain. However, local lesions are often accompanied with impairment of sensation within the sensory distribution of the nerve, for instance in the mouth, loss of corneal reflex or numbness of the skin.

Trigeminal neuralgia (tic douloureux) is of unknown etiology and usually occurs in persons more than 50 years of age. It may occur in an occasional person after the age of 40 years

The chief symptoms are the intense, unilateral, darting pains which radiate from the side of the nose or the upper lip, through the teeth, or into the eye, or even into the forehead and head. The pains come in paroxysms, lasting for a few minutes, during which the face is flushed and the eyes and nose run. There is an expression of agony. The patient, once the disease has started, is seldom free from some pain, and a breath of cold air, speaking, eating or putting out the tongue may bring on a paroxysm The pains may come on for a certain length of time each year, often during the beginning of cold weather.

On examination there may be observed spasmodic movements of the face or jaws There is no disturbance in the functions of the trigeminal nerve in either the sensory or the motor spheres. At the sites where the divisions of the nerves pass through the fascial sheaths, on the upper lip and in the mouth may be observed a so-called trigger point. On stimulation of a trigger point, pain immediately ensues. The employment of ice for the precipitation of pain in one of these patients is a cruel practice

nerve supply to a portion of the skin Eating or drinking is accompanied by excessive perspiration in the area in which the nerve supply has been impaired Langenskiold offered what he believed to be a satisfactory explanation of this distressing symptom· the preganglionic sympathetic fibers governing sweating had been destroyed, thus, according to Cannon's law, the postganglionic cholinergic fibers were rendered hyperexcitable, and during mastication acetycholine elaborated in the parotid gland "diffundated" to the nerve endings in the skin and produced sweating. Gustatory asymmetric hyperhidrosis may occur below the neck as described by Mellinkoff and Mellinkoff.

THE MUSCLES OF THE FACE

Facial Spasms. Spasmodic contraction of the facial muscles may be tonic, that is, continuous, or clonic, that is, intermittent It may be unilateral or bilateral and may involve one or all of the muscles which are innervated by the facial nerve. In order to form an opinion of the cause of spasmodic affections of the face, it is advisable to take into consideration the age and sex of the patient and to ascertain the presence or absence of disease of the eyes, teeth and skin. In some cases the facial symptoms constitute a significant part of a disease of the central nervous system.

The diseases or conditions which may be indicated by facial spasm are mimic spasm, convulsive tic, blepharospasm, nictitating spasm, exophthalmic goiter, chorea, epilepsy, tetanus, meningitis, hysteria, spasm following paralysis, irritation at the root of the facial nerve and, finally, lesions of the cortical center of the facial nerve.

Mimic spasm is usually bilateral and ordinarily does not begin until adult age A more or less constant twitching of one side of the face, with partial closing of the eye, occurring in an adult, is a mimic spasm

Habit spasm usually occurs in neurotic children Characteristically, during the spasm there is a sudden wink of the eye or a rapid drawing of the mouth to one side or a sniff occurring at irregular intervals and greatly intensified in severity by emotional causes

Convulsive tic ordinarily is a hereditary affair occurring in neurotic children The tic is irregular movement of the facial muscles and frequently those of the arms, and sometimes is accompanied with an explosive ejaculatory utterance of profane or obscene words, or this tic may consist of involuntary repetition of a word or the mimicking of an action.

FACIAL PAIN

Infections of the sinuses and the antrums cause facial pain Dental neuritis, particularly when it occurs in senile patients, is troublesome and unfortunately is not readily relieved Often improvement of the general health of the patient by appropriate dietary regimens ameliorates the complaint. The *localized dental neuritis* that follows procaine block injections is due to the excessive amount of procaine injected into the immediate vicinity of the nerve The symptoms of paresthesia usually disappear. Postherpetic *ophthalmic neuralgia* is persistent, and its course is not affected by operative procedures Snake venom may help.

The neuralgias are common causes of pain in the face In *glossopharyngeal neuralgia* the pains are projected along the distribution of the ninth cranial nerve. The trigger zone is situated in the tonsillar fossa, and the darting pains are projected toward the ear, usually terminating in the tympanum. The pains are precipitated by yawning, swallowing and talking, but not by rubbing the face The pains resemble those of trigeminal neuralgia in their occurrence, duration, repetition and character, but they differ from those of trigeminal neuralgia in their distribution In glossopharyngeal neuralgia it will be observed that cocainization of the pharynx will result

The infection as it occurs in children is not a serious one There are moderate fever and mild congestion of the nose and throat which precede the swelling of the parotid glands. The pain in mumps is produced by increased glandular activity. This fact accounts for the time-honored procedure of a test for mumps, favored by grandmothers for many generations, of having a child who is suspected of having mumps bite a pickle. After the age of puberty mumps is a more serious disease, especially in boys and men, because of the frequent and painful complication of orchitis which may lead to testicular atrophy and to sterility. Oophoritis is less serious because the inflamed and edematous ovaries are not confined by a thick fibrous tunica like the testicles in adolescent boys or in men. There may be a minimal involvement of the parotid glands, the first symptoms being those of orchitis, which in mumps may be either unilateral or bilateral. The orchitis often is accompanied with acute severe pain, and there may be a high fever. In women a mild mastitis may occur.

EXAMINATION. There may be either a unilateral or a bilateral enlargement of the parotid or submaxillary glands or none discernible on examination Swelling of a gland usually reaches a maximum within 48 hours after onset and most often persists for 7 to 10 days. Occasionally, some enlargement of the glands of salivation can be discerned after the lapse of several weeks

In the earlier stages a restricted area of redness may be observed immediately about the orifices of the ducts of Stensen and Wharton Fever of moderate degree may be present 12 to 24 hours before swelling is observed, and it usually persists from 1 to 3 days. In many cases fever is absent.

The most important findings on examination in mumps are those indicating involvement of the epididymis and testicle This may be bilateral or unilateral, and when bilateral, sterility often ensues. There are exquisite tenderness, pain and swelling of the testicles. If the testes are involved on subsidence of the swelling, atrophy may be observed either unilaterally or bilaterally. On the basis of studies on changes in the blood diastase and amylase, some degree of pancreatic involvement is often revealed Physical findings may reveal evidence of encephalitis during the course of mumps (see Diseases of the Brain, Chapter 15).

The total leukocyte count may be moderately elevated or depressed but is usually within normal limits The differential count may reveal an absolute or a relative increase in lymphocytes from the first to the fourteenth day of the illness In contrast to the blood, the leukocyte count of the cerebrospinal fluid is of great significance in the diagnosis of the general syndrome of aseptic lymphocytic meningo-encephalitis, of which mumps virus is one of the known etiologic agents In mumps encephalitis the number of white cells of the fluid is increased The total count may range from normal to more than 2,000 per cubic millimeter. In a majority of cases the proportion of lymphocytes is from 90 to 100 per cent It is known, however, that in apparently uncomplicated encephalitis a moderate or marked increase in lymphocytes may occur in the spinal fluid A specific complement-fixing antibody may be present in the blood of adults and children who deny having had mumps

DIAGNOSIS Often the parents or the grandmother has diagnosed mumps correctly before the physician is consulted, if he is consulted at all The diagnosis in sporadic cases is difficult, for it is necessary to differentiate mumps from suppurative parotitis, enlargements due to foreign bodies in the salivary ducts, neoplasms, Mikulicz's disease and uveoparotid fever. The possible complications are numerous, and appropriate diagnostic examinations and procedures will depend on the existing complication

It is now possible to obtain serologic evidence of any type of infection caused by mumps virus. This can be accomplished by demonstrating the appearance of or increase in an antibody capable of fixing complement in the presence of mumps

antigen, and by the demonstration of the appearance or increase of a specific factor, antihemagglutinin, in the blood serum which inhibits the agglutination of chicken or human erythrocytes by mumps antigen. The first procedure is recommended

As with many serologic tests, a definite diagnosis can be made only as the disease progresses and there is a significant rise in antibody titer, revealed by successive examinations of the blood following the onset of the disease.

Chronic Inflammation. Chronic inflammation of the parotid gland may remain symptomless When symptoms do occur there is a sudden swelling and pain of the gland which commences during a meal. The swelling and pain subsides in 3 to 4 hours.

On examination during the attack the gland is greatly enlarged and tender and no secretion is discharged from the duct. Between attacks the secretion is thick and glairy Subsequent attacks may occur, frequently they do not The glands may be enlarged

Tumors. *Mixed Tumors.* Mixed tumors of the parotid gland are hard, usually ovoid and lobulated, and are situated in front of the ear and below it Tumors of this type invariably develop in the lower half of the gland, whereas adenomas and primary malignant growths of the parotid gland usually originate in the upper half of the gland. In their early stages mixed tumors are situated within the gland substance and consequently are not freely movable. The adenomas are freely movable until they become malignant.

Mixed tumors of the parotid gland develop in a congenital anomaly and seldom are discovered before early adult life. Usually such a tumor is not seen by the physician until years have elapsed and the patient has known of its presence for a long time As the tumor enlarges, it causes a rounded induration in the parotid region Situated as it is within the substance of the gland, the tumor in the course of growth sometimes causes a stretch on the facial nerve, so that partial paralysis of the nerve takes place Complete facial paralysis as the result of a parotid tumor is unusual, however, even if malignant changes have occurred within the tumor If the mass attains a large size, the skin over it may become ulcerated The ulceration causes very little pain A mixed tumor of the parotid gland grows slowly; its size is not an indication of whether or not it is malignant, and palpation will not determine this point. A search for affected lymph nodes in the region, therefore, is important.

Mixed tumors that lie superficially to the parotid gland tend to form pendant growths; in other words, tumors thus situated grow away from the gland rather than within it.

Adenomas and Cysts. Adenomas are fairly common in the parotid gland, where they begin as simple, encapsulated nodules of gland tissue As stated, they tend to occur in the middle and upper parts of the gland, seldom in the lower pole These cystic, glandlike tumors become malignant much more frequently than do the mixed tumors of the parotid gland Prior to the malignant change they grow slowly.

Carcinoma. Carcinoma of the parotid gland often begins within the normal gland tissue or in adenomas If a simple parotid adenoma has been incompletely removed surgically, the remaining adenomatous tissue seems to be a favored site for malignant disease, and a carcinoma occurring in such tissue has a bad prognosis. Carcinomas in adenomatous rests, or within the gland substance, become extensive regions of infiltration, involving much of the gland and the tissues beyond it. Carcinomatous tumors of the parotid gland are hard irregular masses but they cannot be diagnosed by palpation. They are diagnosed by histologic study of biopsy material The prognosis in malignant disease of the parotid is always serious.

THE LIPS

Thick lips or thin lips are often a racial characteristic, as in the Negro (thick) or the American Indian (thin) (see Races, Chapter 16). Tradition has it that full

lips in white races mark a phlegmatic temperament. The lips are thickened and coarse in myxedema and cretinism

The color of the lips is often significant of anemia and other conditions in which the skin is pallid, and the first evidence of cyanosis is often seen in them, their slight blueness attracting attention to the existence of cardiac or pulmonary disease.

Open, and particularly *dry and cyanosed, lips* are likely to indicate dyspnea. Open lips may be due to disease within the mouth: stomatitis, glossitis, cancrum oris, phlegmonous tonsillitis, or some form of nasal stenosis. Loose and pendulous lips in a very ill patient are suggestive of a central nervous system disorder, that is, early hemiplegia or bulbar palsy. The open mouth is seen in some normal persons, in all conditions of great prostration, and in idiots and some insane persons.

Trembling or twitching of the lips may be a symptom of general nerve fatigue, paralysis or chronic bulbar palsy. Convulsive raising of the upper lip, with an accompanying squinting of the eyes and wrinkling of the forehead, is occasionally evidence of great pain.

The term *macrocheilia* implies thickened lips. The condition is observed in children, and usually the increase in size of the lips is due to an increase in the muscle and connective tissue. In this condition the lips seem to be less prone than the tongue gradually to increase in size. When the lips have attained two or three times their normal size, the growth ceases and the size remains stationary. The increase in size may be so little in evidence that the disorder is neglected until the child reaches a self-conscious age. This great increase in the size of the lips, occasionally accompanied by increased size of the tongue and the cheek, is very much like the increases in size seen in hemihypertrophy which may involve a whole side of the body.

Unilateral deviation of the lips, the angle of the mouth being drawn to one side and downward, if not due to loss of teeth on the opposite side or to the contraction of scars, is indicative of facial paralysis, either existing alone or as a part of a hemiplegia.

A brawny, hot *swelling of the lip* may be a small abscess or a more extensive and serious carbuncular inflammation The lips are swollen as a part of the disease in the fortunately rare cancrum oris Swelling may be due to the taking of corrosive poisons, in which case the interior of the mouth will also be swollen and reddened. Bites of insects may explain a swelled lip, and among other causes are alveolar abscess, bitten lip in epileptic or other convulsive disorder, and angioneurotic edema

Foam on the lips is a common symptom during an epileptic seizure, and sometimes in the later stages of cerebral apoplexy and in pulmonary edema. It should be borne in mind that a bit of soap in the mouth is employed by malingerers in simulating epileptic convulsions

Malformations. The zone indicating the meeting of the median nasal processes during development is normally evident by double ridges and a shallow groove passing downward from the nasal septum to the margin of the upper lip; the *philtrum.*

A median defect of the upper lip or jaw, through incomplete union of the median nasal processes, is a rare anomaly An equally rare anomaly is imperfect fusion at the midplane between the mandibular processes which form the lower lips and jaw A slanting cleft may extend from the mouth up the cheek. It is due to the failure of union between a maxillary process and the nasal processes.

Cleft Lip or Harelip. This is a common disfiguring congenital deformity of the face. It is so named because of its resemblance to the lip of a hare. It is frequently associated with a cleft of the soft palate or the hard palate or both. The deformity is the result of a failure of union of the embryologic components that after union differentiate the nasal and buccal cavities The first or mandibular arch very early in embryonic life becomes separated into a short upper maxillary process and a

longer, lower mandibular process. The maxillary process together with that of the other side and the intervening portion known as the premaxillary (frontonasal) process, which has descended in the median line from the head, unite and form the superior and lateral boundaries of the oral cavity and the nose If the premaxillary process unites with only one maxillary process, a unilateral cleft is found, but if it unites with neither, a bilateral cleft is present, the premaxillary process extends forward as a proboscis, and a cleft exists in the alveolar ridge. It can thus be seen that all gradations of a deformity may exist from a slight V in the lip to a complete cleft of lip, alveolar ridge and palate. The main symptom of harelip and cleft palate is nasal voice On examination the degree of disfigurement is proportionate to the degree of the congenital deformity. The diagnosis is obvious.

Inflammations. Inflammations of either the upper lip or the lower lip may be the result of any ordinary pyogenic infection which has entered the lip through an abrasion The *staphylococcus* is a common offender in these inflammations.

Inflammation of the lower lip is not nearly so important clinically as inflammation of the upper lip, since a localized furuncle or a diffuse inflammation of the upper lip may extend and produce a sinus thrombosis with subsequent death of the patient Any inflammation of the upper lip of any magnitude at all should be considered as serious These lesions are much more serious in their import than are the malignant tumors of the lip, which have received much more attention from members of the medical profession

Herpes (Virus Infections) The herpes virus infections of man occur in a variety of clinical types. Herpes simplex groups of viruses may cause (1) diseases of the skin, (2) diseases of mucous membranes, (3) diseases of the eyes, (4) diseases of the nervous system and (5) herpes progenitalis.

One of the commonest lesions of the lip is *herpes febrilis*. The etiology of herpes febrilis, the common herpetic vesicles or coldsores or fever blisters, is a filtrable virus that can be demonstrated by inoculating the corneas of rabbits The virus of herpes febrilis (herpes simplex) has been thought to be identical with that causing encephalitis lethargica, and consequently it has been studied intensively

The patient who has a recurrent attack of fever blisters is as a rule singularly free from severe systemic symptoms It seems that such persons have become carriers of the virus and are likely, after nonspecific stimuli, such as fever, menstruation or emotional upsets, to have recurrent manifestations of herpetic infection.

The lesion of herpes simplex is heralded by a feeling of irritation or burning pain in the area of skin involved Erythema quickly followed by papulation and vesiculation ensues in this area The vesicles are grouped, thin-walled lesions which rupture soon, in from a few hours to a day The lesions may occur anywhere on the skin, but definitely tend to appear most commonly at mucocutaneous junctions, on the lips and on buccal surfaces of the mouth, and to recur in the same sites The lesions heal without scar formation

Fissures. Fissures of the lip sometimes follow trauma Less often, a fissure remains after the healing of herpes labialis. Generally fissures of the lip result after prolonged drying of the mucosa as a consequence of being out-of-doors in the heat and sun and dust most of the time, or inside where there is considerable drying of the lips from exposure to high temperatures and low humidity. Fissures may remain as such, or they may become ulcerated

On examination of a chronic fissure it is seen that the fissure has formed and has healed again and again, without there being any manifestation of malignancy. However, although a fissure may remain for years without notable change, malignant degeneration may begin at any time along its borders Unless a fissure is picked with the finger nails, it usually does not bleed. When a fissure begins to bleed rather easily it is time to consider that a cancer may be arising in the cleft.

Fissure of the lip may become painful, the patient complaining of the pain, for example after taking a chew of tobacco or a dip of snuff, when the tobacco-laden saliva gets into the fissure.

Perlèche. Perlèche, as the term is now employed, usually denotes the changes at the angles of the mouth which occur in vitamin B complex deficiency. However, idiopathic perlèche and pseudoperlèche do occur.

Idiopathic perlèche includes instances of perlèche encountered devoid of concomitant clinical or laboratory findings, which, in the light of present knowledge, must simply be considered as of idiopathic origin. In some instances there is an accompanying salivary drooling, or possibly excessive or chemically altered salivary secretion in association with scrotal tongue, with geographic tongue or with macroglossia.

Pseudoperlèche includes those instances of contact dermatitis, neurodermatitis, seborrheic dermatitis, atopic dermatitis, severe chapping and herpes which occur in the region of the oral commissures, and because of the movement in this area by mastication and talking perlèche-like fissuring ensues. Perlèche-like involvement is also seen at times in the rhagades of congenital syphilis and as an extension to this area from mucous patches of syphilis in the mouth Transitorily, perlèche-like involvement may result from the trauma of manipulations incidental to dental therapy.

The symptoms of perlèche are mild, usually consisting merely of a feeling of dryness and at times a slight burning sensation. Deep, infected fissures may be painful and, though rarely encountered, occur chiefly in perlèche of adults.

Objectively, the epithelium of one or both labial commissures is somewhat macerated, either adherent or easily detached, and wrinkled. Later the wrinkles become deeper, often forming one or more transverse fissures with little if any tendency to bleed. The involvement usually stops rather abruptly just within the mucocutaneous junction of the commissure, but extends as a localized erythematous scaling dermatitis, usually with fissuring, from a few millimeters to as much as 2 cm or more outward and downward from the mouth angle onto the skin of the lower lip Untreated, the lesions in all types of perlèche have a tendency toward spontaneous remission and exacerbation, but they rarely disappear completely.

Pyogenic Ulcers. Pyogenic ulcers of the lips are a not uncommon end result of various traumas to the lips. Some of these ulcers result from direct trauma, such as a blow to the lip from a fist or being thrown against the windshield in an automobile accident On examination the elevated surface is soft to touch and the whole lesion is soft when it is grasped between the fingers. If the lesion is of long duration, it may be hard on palpation Very little bleeding occurs from manipulation and handling of these lesions, and the adjacent tissues are but slightly hyperemic.

Some of these ulcers may be tuberculous in origin Tuberculosis of the lip occurs on the vermilion border without a like lesion elsewhere in the mouth. Biopsy may be required for diagnosis

Benign Ulcers. Benign ulcers occur either on the upper lip or on the lower lip. On examination these spontaneous ulcers usually are manifested only by a defect in the epithelium Such lesions may continue for months, even years, without noticeable change, or they may heal, only to recur Recurrent lesions may end in malignant disease Ulcers of this type sometimes occur on the lower lip, but not usually [illegible]

[illegible]

[illegible] frequently are on the upper lip. Malignant lesions, on the con-

trary, commonly occur on the lower lip. Chancres develop and may attain considerable size within a few weeks Carcinomas of the lip do not progress so rapidly.

On examination a chancre of the lip, if it has been present for some time, has an indurated feeling to the examining finger, and it is elevated and may be sharply circumscribed. If a chancre is examined in its early stages, it is a small nonelevated lesion with but little induration about its edges.

Positive serologic reactions of the blood or the spinal fluid, conjoined with an ulcer of the lip in a young person, may be presumptive evidence that the ulcer is a chancre Positive serologic reactions, with an ulcer on the lower lip in an older person, may not be of diagnostic significance.

Lesions which are the result of undernutrition may appear on the lip as punched-out ulcers, and it is likely that similar lesions will be found on the tongue or elsewhere in the mouth

Wounds. Wounds of the lips when properly approximated heal readily because of the free blood supply. This free blood supply also accounts for the extensive swelling which occurs after injury or infection, the latter, however, only rarely occurring after injury

Tumors. The commonest tumors of the lips are the benign cysts that form in the glands of the mucosa These are small bluish tumors occurring near the vermilion border, more frequently of the lower lip On examination the dome of the benign cyst is firm and uniform in outline, and it may or may not be translucent.

Lymphangiomas. Some of these lesions are congenital in origin but may not be manifested during the first several years of life. They may occupy a part or all of the lip Although soft to touch, they are not reduced in size by pressure. If a lymphangioma results from trauma, as is often the case in middle-aged persons, there is a firm region which is due to the scar which resulted from the trauma. There is little difficulty encountered in the diagnosis of the lymphangiomas of congenital origin, for they are uniformly boggy and compressible to the touch without being reducible in size Some lymphangiomas of the lip attain enormous size and are grossly disfiguring.

Angiomas. In infants the blood vessels, mainly the veins, of the lips sometimes become enlarged, forming a large protrusion. The initial enlargement may be noticed at birth or soon after birth as a dusky blue, slightly swollen spot on the lip. As the child grows, the swelling enlarges, sometimes rapidly.

Hemangiomas. These lesions are of congenital origin and are always reddish or purple. On palpation they are soft and compressible and are reduced in size or obliterated by pressure. In children they may be increased in size when the patient cries or coughs, also in adults who have extremely large hemangiomas on the lips, coughing increases the size of the tumors.

Cutaneous Horns. Cutaneous horns of the lips are labial lesions common in advancing years; they may occur, however, in young adult persons Cutaneous horns of the lips do not differ from cutaneous horns on any other part of the body except that on the lips they are more likely to become malignant than elsewhere. Over the rest of the body the horns may occur in successive generations and be shed

The first appearance of a cutaneous horn is a small elevation hard to the touch with a sharply defined base. Occasionally a cutaneous horn will develop on the base of an ulcer or in a fissure or a granuloma These horns vary considerably in consistency, one part may be very hard and cornified, and another part may be granulomatous Some of the very small horns may be moderately hard. They grow in length rather than in diameter, consequently their name When inflammation exists around the base of these tumors, it should excite suspicion that the tumor is malignant. It is remarkable how long a patient will put up with one of these long excrescences on the lip. In generalized cutaneous horns there is no known treatment Roentgen therapy is not effective.

Pigmented Moles. Occasionally along the mucocutaneous border of either the upper lip or the lower lip there will be a darkly pigmented mole. Under no circumstances should a specimen of such a lesion be taken for biopsy. These moles are potentially malignant. Some of them are highly malignant (melano-epitheliomas).

Cancer. Cancer or epithelioma of the lip almost always affects the lower lip rather than the upper lip. It is commonly *secondary to a chronic fissure, leukoplakia* or *keratosis* of the lip, and it is a disease usually of middle-aged farmers who are exposed to sun, wind and drying of the lips These lesions are hard, indurated, ulcerating or bleeding, and often produce considerable stiffening of the surrounding tissues.

The disease extends through the lymphatic channels, which pass down and out from the lips to the submaxillary lymph nodes and then to the nodes along the great vessels of the neck. It is in these regions that the lymph nodes are affected by the spread of cancer from the lip. The middle of the lower lip drains into a node in the submental region in front of the submaxillary nodes Finding this node enlarged is not of much significance, for it frequently is enlarged when there is no demonstrable lesion of the lip Enlarged nodes may be found on both sides of the neck and are secondary to cancer of the lip.

A *primary cancer of the lip* is defined as one developing without a previously existing fissure or ulcer. It occurs more frequently in men than in women, and about 10 times as frequently on the lower as on the upper lip. Cancer of the lower lip is almost invariably of squamous cell type. On the upper lip it frequently represents invasion of the lip by a carcinoma of the skin, and may be either squamous cell or basal cell carcinoma.

Primary cancer of the lip is a localized, hard, deep-seated lesion of firm density, and is unyielding on pressure Examination of the epithelium over the lesion reveals that the surface is being approached or that there already is ulceration. When ulceration of these lesions occurs, there is free bleeding on the slightest trauma; palpation of these hard ulcers causes them to bleed A patient may be unaware of the seriousness of an ulcer on the lip until the ulcer begins to pain or to become deeply ulcerated, or the lymph nodes under the jaw become ulcerated

Liljencrantz classifies cancer of the lip by stages in its development determined on examination· clinical stage I: lesion less than 1 cm. in diameter without muscle infiltration; stage II moderate-sized lesion (1 to 3 cm. in diameter), usually accompanied by early muscle infiltration, stage III large lesion (more than 3 cm in diameter) with deep infiltration, and all lesions with involvement of bone or cervical lymph nodes

Cervical lymph nodes may contain cancer cells and not be enlarged Ulcerated, infected primary lesions often cause inflammatory hyperplasia, and it is frequently impossible to distinguish clinically between inflammatory and metastatic cervical nodes

Biopsy establishes the diagnosis Any ulcer, fissure, scaling, heaped-up or papillomatous lesion remaining on the lip for more than one month should be suspected of potential malignancy. Inspection and gentle palpation are most important in making a clinical diagnosis A negative blood serologic reaction and absence of history rule out coexistent syphilis A positive serologic reaction does not exclude cancer and should not be the cause for delaying biopsy

THE MOUTH

Surface Anatomy. In looking into the mouth one sees the tongue below and the roof above, surrounded in front and on the sides by the teeth On each side are the inner surfaces of the cheeks and posteriorly are seen the uvula, the arches of the palate and the pharynx On the mucous membrane of each cheek, opposite the second upper molar tooth, is a small papilla through the top of which opens the duct of the parotid gland A small probe can be inserted into the duct from the oral cavity and passed outward and backward toward the gland.

Size of the Mouth. The primitive slit may fail to reduce normally (macrostomia); on the contrary, the degree of closure may be excessive (microstomia). Size of the mouth also seems to be hereditary.

The Buccal Cavity. Odor of the Breath (*Halitosis*) There are many variations from the normal in the odor of the breath. Local conditions in the mouth may be accountable for an unpleasant or foul odor of the breath. In dehydration, when sordes have collected on the teeth, the breath is likely to be stale and musty. A foul odor attends in some degree all forms of stomatitis and glossitis, and is most fetid in the mercurial and gangrenous forms. Caries of the teeth, necrosis of the jaw, pharyngeal or tonsillar diphtheria, follicular tonsillitis and lacunar concretions are local conditions that may explain the existence of unpleasant emanations. Frequently a bad breath attends migraine headaches and chronic alcoholism A hot feverish breath is common in febrile disorders An ammoniacal, urinous odor is not uncommon in the severer grades of uremia. A heavy, sweetish odor is perceived in bad cases of diabetes mellitus, often preceding or accompanying diabetic coma

It is well to recall, however, that the normal human breath is odorless and that many instances of halitosis are the so-called essential halitosis. It has been said that man's breath becomes infected by the bad quality of food, by the bad state of the teeth and still more by old age At one time or another during life everyone suffers from malodors coming from the mouth. The presence of offensive breath does not cause pain or other subjective inconvenience If the patient is aware of halitosis, it may be the cause of deep despondency which arises because in most instances the foul odor is not at all recognized, or at most only partially so, by the patient

There is a popular opinion abroad that bad breath originates most frequently from disorders of the stomach and colon—constipation. Gas cannot pass from the stomach or from the intestine back through the collapsed esophagus under normal conditions except in belching In certain diseases of the esophagus in which there is retention of food in a dilated portion or in a diverticulum, there may be foul odors on the breath Pyloric stenosis and the late stages of cancerous ulceration of the stomach are productive of pronounced foul odors. In cases of fecal vomiting and gastrocolic fistulas a fecal odor of the expired air may be observed

Dryness of the Mouth. Dry mouth due to diminished secretion of saliva may lead to redness, soreness and fissuring of the mucous membranes, and if long-continued, eventually to atrophy In severe instances rapid deterioration of the teeth follows Chewing and swallowing may become difficult Inadequate amounts of saliva, according to Allington, may result from (1) a decrease in salivary gland substance (congenital hypoplasia, senile atrophy, destruction following surgical intervention, irradiation, inflammation or neoplastic infiltration), (2) disturbances of innervation (central or peripheral nerve lesions, emotional states, psychoses, interference with conduction of nerve impulses due to drugs, toxic agents or metabolic disturbances); (3) dehydration and (4) unknown causes (Sjogren's syndrome). In *Sjogren's syndrome* dry mouth is associated with dryness of the eyes and of the mucous membranes of the nose, throat and vagina and with deficient gastric secretion. Many of these features suggest deficiencies of vitamin A, nicotinic acid and riboflavin, and some of them are seen in pernicious anemia, iron deficiency anemia and *Plummer-Vinson syndrome*. There is a frequent association of the syndrome with rheumatoid arthritis and with the endocrine changes that occur in postmenopausal women. In aging men after many years of excessive smoking, chewing of tobacco or dipping snuff, dry mouth is common. Treatment of dry mouth must be directed toward the causative factor.

Salivary Taste Hormones. Dryness of the mouth from any cause often impairs taste Reasons for this clinical observation are partially accounted for by dryness of the mouth in some, and in others by the hereditary absence of salivary taste hormones It seems that most persons can taste saccharin and sodium chlor e on a

wet tongue, but some cannot taste these substances on a dry tongue. Cohen and Ogdon have demonstrated a salivary taste hormone which could account for these discrepancies of taste on dry tongues and in some a normal absence of this hormone.

The Sense of Taste. The four primary taste sensations are bitter, sweet, acid and salt.

Taste buds, the end-organs of the gustatory sense, cannot be identified grossly. They are scattered over the mucous membrane of the mouth and tongue at irregular intervals, and occur especially in the sides of the vallate papillae. They decrease in number gradually during adult life and rapidly in extremely old age.

The taste fibrils run in both the glossopharyngeal nerve and the trigeminus nerve, the former supplying the posterior third of the tongue, the latter the anterior two thirds. A complete loss of taste may result from trigeminal disease alone, and occasionally from lesions affecting only the glossopharyngeal nerve. It seems, therefore, that the gustatory fibers may at times be present solely in the trigeminus and at other times solely in the glossopharyngeal nerve Some of the taste fibers may pass by way of the chorda tympani, since a partial loss of taste may be present in facial paralysis. Ordinarily, a solution of sugar is sufficient to enable one to detect any impairment of taste.

The disorders of the gustatory sense are ageusia (loss or impairment of the sense of taste) and parageusia (perversion of the sense of taste)

AGEUSIA. Impairment or absence of the sense of taste may be due to local unhealthful conditions of the mucous membrane of the tongue. If the tongue is dry, taste is much lessened or abolished. Since the sense of smell plays a considerable part in the production of the sensations ordinarily referred to the sense of taste, a patient who has acute coryza or bad colds may complain of a loss of taste Large doses of the bromides blunt the sense of taste.

The lesions affecting the sense of taste may be basal meningitis, tumors and injuries. Ageusia may be one of the manifold symptoms of hysteria, which, with facial paralysis, is the commonest cause of a partial loss of the sense of taste. In each case associated symptoms must determine the diagnosis.

PARAGEUSIA Purely subjective perversions of the sense of taste are usually indicative of hysteria, they may constitute the aura of epilepsy; in the insane they may be hallucinations. Various bad tastes frequently are a source of complaint of neurotic patients. The administration of certain drugs may give rise to disturbed taste sensations.

Petechiae. Small extravasations are occasionally seen on the buccal mucous membrane, and when present, may be caused by one of the grave anemias, hemophilia, purpura hemorrhagica or scurvy; or they may be the hemorrhagic infarcts of ulcerative or septic endocarditis.

Exanthems, Erythema and Vesicles. The rash of measles is often seen on the pharyngeal and palatal surfaces prior to its appearance on the skin, and Koplik described, as absolutely characteristic of measles, small red spots with minute blue-white centers on the inner surface of the cheeks which disappear as the rash develops. The angry redness of scarlet fever, involving the entire oral and faucial surfaces, is very striking A slighter redness is present in simple erythematous stomatitis, and the rare occurrence of a salivary calculus with accompanying redness should be remembered Vesicles when present may be the beginning of an aphthous stomatitis, herpes, the eruption of varicella or smallpox, pemphigus or recent burns.

Pigmented Spots, Ulcers and Sloughs. Dark spots, usually of various shades of brown, occur in dark-skinned races or in mixtures of white and black races All of those diseases such as Addison's disease which cause a darkening of skin color may be manifested by dark spots in the mouth

Small grayish ulcers with reddened margins, which have begun as vesicles situated on the inside of the lips and cheeks and on the edges of the tongue, are the lesions of aphthous stomatitis, the common canker sores. If removal of exudate on the gums, buccal surfaces, tonsils or soft palate reveals ulcerations, the exudate may

be due to Vincent's angina. White, curdlike patches, beginning on the tongue ar
spreading to the inside of the lips and cheeks and leaving, if detached, a normal
slightly ulcerated surface, form the disease known as thrush Aphthous lesions
the mouth, recurrent ulceration of the genitals accompanied by iridocyclitis fo
lowed by hypopyon constitutes Beçhet's syndrome. The etiology is unknown.

Salivation and Dribbling. The amount of saliva which is secreted in 24 hou
is, under normal circumstances, from 1,000 to 1,500 ml Ptyalism or hypersecretio
of saliva, in which this amount is greatly exceeded, may occur in early pregnanc
dementia praecox, encephalitis, rabies and sometimes attends the menstrual perio
The pain due to dental causes, alveolar abscess, or trigeminal neuralgia, and th
process of dentition itself, will induce an excessive formation of saliva Dribbling c
saliva may occur as a result of hunger and, at times, because of inability to retai
saliva, as during sleep

Stomatitis. Stomatitis often accompanies infectious diseases such as scarlatina measles, influenza, typhoid and rickettsial fevers and botulism The blood dyscrasia and certain forms of avitaminosis may cause pathologic changes in the mouth During the eruption of the temporary or milk teeth there may be stomatitis. From the standpoint of general medicine, catarrhal gingivitis, catarrhal stomatitis and so-called aphthous stomatitis should be looked on as a complication of many and various disease conditions that are manifested in the mouth

Epidemic Stomatitis (So-Called Foot and Mouth Disease). Epidemic stomatitis is a disease of cattle and goats that is highly communicable to man. It is characterized by [illegible] in temperature and by eruption of vesicles on the mucous membranes of th[illegible] filtrable virus which is present in the fluid contents o[illegible] kidneys, the salivary glands and the mammary glands [illegible] the mouth Occasionally the virus may produce the disease by entry [illegible] The period of incubation lasts from 3 to 10 days

In the early stages of the infection there may be slight fever, chills, headache, muscular pains and general malaise These symptoms are followed by the characteristic manifestations, which are swollen, painful lips and a thick, coated tongue showing imprints of the teeth Within 2 or 3 days yellow vesicles appear over the soft tissues of the mouth, rarely on the hard palate There is profuse salivation In severe infections, 2 or 3 weeks after the onset of the disease, large vesicles may develop on the hands and sometimes between the toes. The vesicles may increase in size and coalesce to form blebs Occasionally the vesicles are observed on the lower part of the nose and may extend to involve the eyelids

Acute Herpetic Gingivostomatitis. Acute infectious gingivostomatitis, aphthous stomatitis, catarrhal stomatitis, ulcerative stomatitis, Vincent's stomatitis are the cognomens of this disease

This is a common disease of young children due to the virus of herpes simplex There are fever, irritability, red swollen gums, a vesicular eruption on the mucous membranes of the mouth, oral fetor, and local lymphadenopathy A constitutional reaction is always present but varies in severity; a high fever, temperature from 104 to 105 F (40 to 40.5 C) is common

The commonest finding is a characteristic involvement of the gums which varies from a thin red line along the dental margin to extreme redness and swelling of the gums In the rare infant, infected before the eruption of teeth, the gums escape involvement. Lesions in the rest of the mouth, when seen very early, consist of a few to many small vesicles, which soon rupture, leaving grayish lesions of varying size, single or confluent, that may become ulcers. The tongue and cheeks are most commonly involved

In some patients the tonsillar region is affected early, and the disease resembles acute tonsillitis of bacterial origin Submaxillary lymphadenopathy of varying degree

is extremely common. The disease lasts from 10 to 16 days regardless of therapy. Pain tends to disappear within about 1 week from onset, or about 3 or 4 days before the lesions heal. Scarring is absent or very slight. Swelling of the gums and lymphadenopathy, among the first signs to appear, usually persist for many days after the ulcers heal.

Recurrent Stomatitis. Occasionally herpetic stomatitis recurs. The local lesions are similar to those described in the foregoing paragraphs, but there is a virtual absence of systemic reaction in patients so affected. Virus can be isolated from the lesions, and circulating antibodies are present at the onset of symptoms. The distinction of such lesions from etiologically different but clinically similar types of recurrent stomatitis depends on isolation of the virus or on results of biopsy, or both.

Gangrenous Gingivitis or Noma. Gangrenous gingivitis or noma is an acute progressive gangrenous process of unknown origin primarily occurring in children, usually beginning about the buccal gingivae and spreading rapidly to the mucous membranes of the cheek. Soon there is extensive sloughing of the adjacent soft tissues about the mouth. The intense rapidity of the progress of the disease, the absence of a line of demarcation within the inflamed area, and the comparative freedom from pain are characteristics of noma The disease is attended with great exhaustion and almost invariably is fatal.

Oral Diseases Due to Physical and Chemical Agents. The oral cavity is frequently exposed to injurious agents The ingestion and inhalation of foreign substances into the oral cavity lead to an accumulation of chemical, physical and bacterial irritants which are prone to settle along the gingival crevices about the teeth. The gingival portion of the oral mucosa is in a constant state of low-grade inflammation if not actual disease.

The different types of structure, ranging from the oral mucosa to the highly specialized and mineralized enamel, account for the great variety of response that is displayed in the oral cavity from the influence of physical and chemical agents. However, there are other channels of entry of noxious agents into the body (see Diseases Due to Physical and Chemical Agents, Chapter 19).

Schour and Sarnat record that localized abrasions of the enamel of the teeth are found in occupations in which workers hold various objects between the teeth while at work, such as tacks, nails, pipes, musical instruments and whistles. Fractures of the enamel and traumatic effects on the periodontal structures also occur. Dust of abrasives such as sand and cement or ordinary powders and pastes used to clean the teeth may cause abrasions. A distinction is made between abrasion and attrition. Attrition is the physiologic wear of teeth incident to age.

Acid fumes deposited on the exposed portions of the teeth react with the enamel, and decalcification results. Similar action on the teeth results from protracted vomiting in which the hydrochloric acid from the stomach decalcifies the enamel. The ingestion of acid carbonated drinks accomplishes more slowly the same end results of decalcification and often caries

A high incidence of tooth decay and caries has been reported among workers who are exposed to sugar dust. The sugar dust is supposed to be deposited along the labial gingival surfaces of the crown where it stagnates and induces abnormal fermentation, and with the aid of bacteria induces acid production and decay of the teeth

Green staining of enamel, pigmentation, has been observed among copper workers Among silver workers there may be a black staining and there are black

bacteria

The exogenous gingival pigmentation of occupational origin is distinguished from

the endogenous brown melanin of the gingivae that is seen normally in the Negro and the mulatto, and in white persons who have Addison's disease. This melanin is situated in the basal layer of the epithelium, whereas coal dust and metal dust accumulate on the surface and penetrate to various depths of the epithelium and sometimes even the dermis. The sulfides of heavy metals are found only in the dermis but become visible as lines about the gingivae. Certain common heavy metals produce the pigmentation of the gingivae that usually, but not always, follows the ingestion or inhalation of the metal That the ingestion, inhalation, or injection of lead or other heavy metal is not sufficient to produce a line is well illustrated in lead poisoning which follows the injection of lead for the treatment of metastatic malignant disease The essential factor is the presence of chronic gingivitis. Lead absorption does not cause inflammation, but rather inflammation brings out the lead line. The lead line is manifested as faint mottled patches of black at the edge of the gum; a fine black line along the entire gum margin or a black line, wider along the margin of the gums. Patches of black or blue-black pigment occur on the cheeks The gingival lines produced by the heavy metals, lead, mercury and bismuth cannot be differentiated one from the other.

Once a poison such as lead and mercury enters the blood stream, it is precipitated as the heavy sulfide in the colon and at gingival margins or into the oral tissues.

The alveolar processes and jaws may be the first structures affected by blood-borne agents. This is exemplified in yellow phosphorus poisoning in which the "phossy jaw" is a characteristic finding, in mercurial poisoning in which the teeth become loose and are eventually exfoliated, and in radium poisoning, which was first diagnosed because of toxic effects on the jaw bones.

In the early stages only the alveolar bone is affected. In mercury poisoning the disease process may be limited to the alveolar portion of the mandible and maxilla and rarely extends much beyond the level of the apexes of the teeth. In the later stages, however, the osteomyelitis may include a greater portion of the jaws and is followed by sequestration.

Lesions of the Mouth in Vitamin Deficiency. Lesions of the lips, gums, tongue and buccal mucous membranes occur as manifestations of deficiency of ascorbic acid and of some of the fractions of the vitamin B complex. These manifestations are seldom found in pure form.

Oral lesions associated with deficiency of riboflavin begin as an oral pallor, followed by maceration and superficial transverse fissuring in the angles of the mouth. These lesions are a type or types of perlèche A superficial denudation of the mucosa may occur and cause the lips to become abnormally red along the line of closure In addition to the cheilosis there are seen fine, scaly desquamations on a mildly erythematous base in the nasolabial folds, on the alae nasi, in the vestibule of the nose and on the ears. Associated with these lesions, keratitis, part of a riboflavin deficiency may be present.

Stomatitis and glossitis appear early in the course of nicotinic acid deficiency disease and they are manifested by swelling and redness of the margins and tip of the tongue. As the disease progresses, the redness becomes more intense until the parts assume a fiery scarlet hue. Ulcerations appear along the sides, the tip and the under surface of the tongue and on the buccal mucosa opposite the molar teeth. The ulcers may be covered with a thick, gray exudate.

The function of ascorbic acid is concerned with the formation and regulation of the intercellular matrix When deficiency exists, gingival lesions or scurvy, occurs. The essential lesion of scurvy is a vascular disturbance which results in swollen and boggy gums that bleed easily, and may progress to actual ulceration. Chewing is difficult and involvement of the alveolar bones causes the teeth to loosen and fall out. The teeth themselves may be affected by the scorbutic process The dentin and enamel become coarse and defective with resulting rapid and early decay of the teeth.

Hemorrhage into the buccal mucosa may result from damage to the vascular epithelium. Lesions of the gums will not occur if the teeth have been extracted.

Mucous Cysts. Mucous cysts sometimes arise from the mucous glands of the mouth and of the tongue itself. The anterior lingual gland often is affected As a rule, these mucous cysts are small and are felt as hard, rounded bodies beneath the mucous membrane. Dermoid cysts occur in connection with the tongue, but very rarely.

Leukoplakia. Leukoplakia occurs principally in men, and is said to occur more frequently in men who smoke than in nonsmokers. This statement, however, is questionable. The condition begins with hyperemia, following which a whitish granular surface develops. This white granular surface may remain stationary for years, or it may extend, or malignant disease may supervene. The beginning of a malignant process is suspected when the whitish areas begin to pile up and form wartlike structures. Without any warning, however, by changes in the white areas, metastatic nodules may appear in the neck, and after their appearance it is found that the leukoplakia has developed into a malignant condition The lesions, before malignant change develops, are soft to the touch; after malignant disease develops, there is a considerable amount of induration, and the border line, which has previously been definite, now becomes indistinct and hard.

Leukoplakia is to be distinguished from the common benign condition of the buccal surfaces of the lips and anterior pillars of the tonsils characterized by multiple small yellowish spots These spots are enlarged sebaceous glands, and the disease is known as *Fordyce's disease* Fordyce's disease is distinguishable from the Fox-Fordyce syndrome which involves the apocrine glands of the axillae and pubis The latter is under endocrine influence. Lichen planus may resemble leukoplakia

SUMMARY OF ORAL CANCER

Carcinoma occurs within the oral cavity considerably less frequently than it does on the lip. In 6 out of 10 who have intra-oral cancers the tongue is involved; 2 out of 10 will have cancer of the floor of the mouth; 1 out of 10 has the lesion on the cheek, and the last 1 will have it on the gums and the soft palate

Intra-oral carcinoma tends to be more infiltrative in regard to both muscle and bone than does cancer of the lip, and carries a correspondingly higher mortality rate. It tends to produce earlier metastasis in the deeper cervical lymph-node groups. These metastatic lesions may be either contralateral or bilateral but rarely ipsilateral.

Leukoplakia, on the lip or in the mouth, must be regarded as an important precursor of cancer A high percentage of tongue cancer is found to be associated with syphilis and leukoplakia Any ulcer, fissure, nodule or papillary growth existing for more than 2 or 3 weeks should be investigated. Thickened patches of leukoplakia are suspected of being malignant when there is any change in their size or texture Of the various inflammatory lesions which appear like ulcerating malignant lesions [illegible] sermann Biopsy

THE JAWS, TEETH AND GUMS

THE JAWS

Familial Fibrous Swelling. Various diseases of the jaws have been called fibrous dysplasia, fibrous osteoma, osteofibroma and ossifying fibroma, which are now regarded as variants of a fibrous dysplasia. Several members of a family may be affected with fibrous dysplasia of the jaws.

The disorder is characterized by massive swelling of the cheeks and jaws beginning during the first three years of life. Dentition is defective. There are no associated symptoms or systemic manifestations unless the lower jaw becomes so large that it prevents closure of the mouth and interferes with respiration and speech.

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nence to the angles of the mandibles. The reflex is obtained by tapping the lower jaw with a reflex hammer as illustrated in Figure 6-71.

The temporomandibular syndrome is a temporal or bitemporal headache originating from the muscles of mastication and from the fibers of the temporomandibular joints (Williams).

Closure of the bite resulting in a dislocation of the stresses on the muscles of mastication may produce pain that is referred to the temporal region. Tearing of the anterior portion of the joint capsule resulting from extraction of molars with the patient under general anesthesia may result in pain in the region of the joint. Closure of the bite will produce a daytime headache, while injury to the joint capsule is likely to produce pain at night when the mandible drops during sleep. Closed bite rarely produces pain Capsular injury is a relatively commoner, but still an unusual, cause of pain in the head.

Spasm. Trismus or lockjaw, a tonic spasm of the masseter and temporal muscles whereby the jaws are held firmly together, may occur as a symptom of trismus neonatorum, tetanus, strychnine poisoning, hysteria, epilepsy or disease of the brain, and is sometimes a reflex from dentition.

Paralysis. In paralysis the masseter and temporal muscles do not contract and there is inability to masticate on the affected side Paralysis of these muscles may indicate hemorrhage into the pons, basal lesions (meningitis, tumor, caries) or neuritis

Pain and swelling from disease of the maxillae, mumps, quinsy or trichinosis may prevent the opening of the mouth and interfere with mastication.

Ankylosis. Ankylosis of the mandible is seen following traumatism or infection to the temporomandibular articulation. A pseudoankylosis may be due to extra-articular disease The ankylosis may be fibrous or osseous. Unilateral ankylosis, if it occurs before the fifteenth year, presents a disfiguring shortening deformity of the affected side.

Malignant Tumors. The ulcerative type of malignant lesion may not be impressive on inspection On examination the border of the ulcer is hard and irregular in outline with varying degrees of fixation Usually the tumor involves one or more of the teeth, very often the affected teeth have been pulled because the tumor has been suspected of resulting from diseased teeth The fungiform type of cancer may protrude as a solid mass, the surface being smooth without noticeable ulceration

In *carcinoma* of the upper jaw there may be a degree of circumscription because an adamantinoma sometimes becomes malignant and protrudes through the gums. Adamantinomas usually can be differentiated roentgenographically.

Sarcoma occurs in the periosteum of the jaws and in the antrums. The early sign of a periosteal sarcoma is the tumorous elevation that is diffuse. The sarcoma most commonly is situated on the lower jaw In this situation it grows more slowly than in the maxilla Sarcoma of the antrum may develop more quickly than a periosteal sarcoma, and may make itself manifest by expanding the bone, then perforating it and spreading to the surrounding tissues Occasionally a sarcoma grows into the nostril and fills it, this development being followed by a foul-smelling bloody discharge. Tumors of this type are highly malignant dangerous growths of poor prognosis

THE TEETH

Dentition. The maxillae and the mandible carry the teeth The temporary or deciduous teeth appear with greater regularity as to order than as to time The permanent teeth arrive as follows first molars, 6 years, incisors, 7 to 8 years, bicuspids, 9 to 10 years; canines, 12 to 14 years, second molars, 12 to 15 years, third molars, 17 to 25 years

Early Dentition. Eruption of the teeth in advance of the usual dates is not of special significance.

Roentgenograms show extensive multilocular rarefaction and pronounced expansion of the mandible. The maxilla is also greatly expanded, but the rarefaction is diffuse rather than multilocular. No other bones are affected. Near puberty, the facial appearance improves, with a progressive decrease in the size of the jaws; by middle age the roentgenologic and facial abnormalities are minimal or absent. Tissue specimens from the jaws show fibrous tissue containing varying numbers of giant cells.

Osteomyelitis of the Jaws. Owing to the variation in the structure of the upper and the lower jaws, osteomyelitis is differently manifested in the two jaws.

In the *upper jaw* the osteomyelitis may be localized about one or more teeth or may affect much of the bone. However, the process rarely extends beyond the alveolar process. The upper jaw is affected by an extension from a tooth or from the frontal sinuses. Rarity of extensive osteomyelitis in the upper jaw is due to a lack of marrow cavity in this bone.

In children, but rarely in adults, infections in an antrum may be severe and the necrosis extend to the alveolar process and the hard palate

In local infections of the upper jaw well-formed spicules of bone may be cast off at once or at intervals of varying length. Only rarely is there an extension to a number of teeth so that a considerable portion of the bone is extruded In such instances the separated part is firm, and is little eroded except in processes due to chemical intoxication, particularly mercury

The *lower jaw* may be affected by an acute process simulating the acute osteomyelitis of the long bones. The localized necrosis due to local infections may remain as such

Local infections of the lower jaw follow infection about the teeth and frequently are associated with the extraction of teeth The wisdom teeth are the chief offenders. The masseter muscles become infiltrated or reflexly spastic, so that the patient cannot open the mouth The edema may involve the submaxillary region and in severe cases suppuration in the deeper planes may occur even to the spread of the infection down the carotid sheath to the mediastinum Spreading to adjacent teeth may occur The removal of the bacterial focus may allow the infection to subside. Infections following injury by certain drugs, notably mercury, arsenic and antimony, may lead to more extensive destruction Even the local use of arsenic in the preparation for filling of teeth may lead to extensive destruction, even to the loss of a part or all of the alveolar process The involvement of the soft parts in local bone infections is usually limited to a local abscess which opens about the gum or beneath the jaw

The marrow cavity in the lower jaw is limited. Its blood supply is enclosed in the inferior dental canal In cases in which the inferior dental artery is occluded there is destruction of a large part or all of the lower jaw, but usually the alveolar process alone is involved, resulting only in the loss of a large part or all of the teeth. Accompanying the involvement of bone there may be chills, fever, pain and swelling of the jaw. The infection may extend to the neck In such cases wide suppuration of the soft parts of the neck is usual and extension down the carotid sheath into the mediastinum may follow In the severer cases death from generalized sepsis may occur

Owing to the density of the bone of the lower jaw, the necrotic bone is extruded more slowly than in the long bones, so that many months, even years, may be required to complete the process of separation

Defective Mobility. *Inability to open or close the mouth may be due to spasm* or paralysis of the muscles of mastication. The masseter, temporal and other muscles concerned in the act of chewing are innervated by motor fibers from the fifth nerve (trigeminus), and spasm and paralysis of these muscles indicate some interference, organic or functional, with the action of this nerve.

The jaw muscles may be tested by desiring the patient to clench the teeth. If the muscles are intact, lateral ridges are thrown up across the face from the malar emi-

Early, extensive or rapid dental caries may be due to rachitis, but occurs also in pregnancy, diabetes and chronic phosphorus poisoning. Usually, however, it is of unknown cause. The influence of carious teeth as a source of irritation or infection causing bad breath and adenitis is obvious

Grinding of the Teeth. Gritting or grinding of the teeth during sleep does not necessarily indicate worms It occurs in children and in neurotic patients and other adult persons who are affected by pain and who for any reason sleep uneasily.

Infections. Infections of the teeth often originate from deeply extending dental caries. Such infections are usually confined to the roots of the teeth and are defined as apical abscesses They are rarely larger than a few millimeters in size.

The infections may not give symptoms In some instances they occur after the tooth has been rendered nonvital by the dentist but more frequently they occur spontaneously. Pain in the affected tooth and swelling and tenderness localized over the area affected are the common manifestations Infections of a more acute character about tooth roots may involve a greater or lesser extent of the adjacent bone and thus cause an osteomyelitis

Tumors of Dentigerous Origin. *Dentigerous cysts* begin insidiously. The patient's attention is not attracted to the presence of the cyst until the expanding jaw produces a deformity. These tumors can be demonstrated on roentgenologic examination. They may become very large and may involve a greater part of the bone, making surgical removal almost impossible because of the softness and fragility of the bone.

Odontomas. Odontomas, tumors of toothlike structure, are closely allied to dental root, or radicular, cysts Although they represent a more mature tissue development, they often complicate radicular cysts. A dense thickening of the jaws represents the physical findings, which point to the occurrence of odontoma. The diagnosis is confirmed by roentgenologic examination.

Adamantinomas. These are epithelial tumors of the jaw originating from epithelial remnants of the enamel They occur in young persons and produce expanding bone tumors which are first demonstrated by roentgenologic examination. Under ordinary circumstances adamantinomas are noninvasive and nonmalignant tumors.

THE GUMS

A *narrow band of bright red inflamed gum tissue* surrounding the neck of the tooth, primarily on the buccal surface, is a characteristic observation in all species of mammals. It is not a recent disease, nor is it the result of so-called present-day perverted methods of preparing and seasoning foodstuffs Mankind now enjoys the greatest variety of the most wholesome foods that has ever been available to any animal This narrowed band of inflamed gum tissue, more pronounced on the buccal surface, bleeds readily on slightest injury and is comparatively free from pain. *Gingivitis* is a more profound infection of the gums than this reddened tissue surrounding the tooth. It is an extension of this normally reddened margin.

Pallor of the gums is noticeable in all forms of anemia *Red and spongy gums* may be caused by carious or illkept teeth attended with abundant tartar. Spongy, red and bleeding gums, perhaps ulcerated, occurring in artificially fed infants may be due to scurvy A similar condition in an older person may be the result of scurvy or combined vitamin deficiencies.

Swollen or spongy gums are met with in many debilitating disorders such as leukemia, pulmonary tuberculosis, diabetes and purpura. Ulceration along the line of the gums, rarely extending to the cheeks or tongue, is particularly characteristic of ulcerative stomatitis. Finally, localized or general redness and swelling may attend the eruption of the teeth and poisoning by chemicals and heavy metals.

Diseases of the Gums. *Acute Ulceromembranous Gingivitis* (*Trench Mouth*) This disease often is called Vincent's infection or trench mouth. The dis-

Delayed Dentition. The most important cause of delay in dentition after the age of 15 years is rachitis, together with other conditions or diseases involving malnutrition, particularly those occurring in the first 5 or 6 months of the infant's life. The delay, if observed, is more significant of the past than of the present status. A late appearance of the teeth may be indicative of cretinism.

Difficult Dentition. There has been much difference of opinion with regard to the influence of teething in causing disease.

Anomalies of Dentition. There may be a congenital absence (anodentia) of some or all of the teeth, or a production of more than the normal number. Supernumerary teeth in abnormal locations (for example, the palate) arise from ectopic tooth primordia which have been displaced. A third dentition has rarely occurred. Sometimes fourth molars develop behind the wisdom teeth. Teeth have been observed in which, owing to a defect of the enamel organ, the enamel was wanting Imperfect teeth are frequently associated with harelip Epithelial remnants of the dental lamina may give rise to cysts of various

in the edge, it may be evidence of inherited syphilis (Hutchinson's teeth). These teeth are likely to be small, to be placed somewhat irregularly, and to stand apart from one another If keratitis and disease of the middle ear coexist, a presumptive diagnosis of syphilis can be made.

Dentated, Furrowed or Pitted Teeth. If the edges of the teeth are *dentated,* malnutrition is likely to be the cause. *Grooves* or *furrows* running transversely across the teeth are indicative of an acute illness during infancy or childhood sufficiently severe to interfere with nutrition of the teeth. *Pitted* teeth, the molars exhibiting the greatest changes, are caused by exposure to fluorine in the water.

Loosened Teeth. Loosening of the teeth in their sockets is associated with spongy, ulcerated or bleeding gums and is often a familial manifestation Movability of the teeth usually is due to prolonged fevers, pyorrhea alveolaris, old age, mercurial stomatitis, scurvy, purpura haemorrhagica, phosphorus poisoning or gangrenous stomatitis.

Caries. The cause of dental caries is controversial Some believe that the structure of the tooth and metabolic and nutritional factors are the primary causative factors in tooth decay Others believe that local factors in the mouth such as bacterial acids, the physical state of the food, mechanical abrasion and a lack of protective action of saliva are the causative factors of tooth decay.

A clear relationship between salivary amylase and the incidence of dental caries seems to exist In persons without dental caries hydrolysis of starch by saliva requires approximately 45 minutes for completion The saliva of those with 4 to 6 cavities will complete the hydrolysis more quickly Without exception the rate of starch hydrolysis increases in direct parallelism with the number of cavities

The presence of fluorine in drinking water seems to decrease the number of cavities (see Fluorine Poisoning, Chapter 19).

Recent investigations cited by Turner and Crane appear to support the importance of local factors, particularly bacterial acids, as a primary causative agent in tooth erosion Furthermore, current studies emphasize the relation of dietary carbohydrate intake to the formation of acids by the oral bacterial flora. The restriction

production of organic acids, particularly lactic acid, by this microorga- sponsible for erosion of the teeth Excessive amounts of acids in the mouth can cause dental erosion; this has been shown in experimental animals ingesting certain carbonated beverages or dilute acid solutions and in patients taking excessive amounts of lemon juice for therapeutic purposes.

will not cure the lesion. If the lesion continues after the tooth has been pulled, it should be suspected of being malignant

THE TONGUE AND THE FLOOR OF THE MOUTH

THE TONGUE

Inspection of the dorsal surface of the tongue is a part of the clinical examination which seldom was neglected by earlier physicians. Perhaps never has so much been said about so little as in the nonsense written about appearances of the tongue as presenting evidence of diagnostic significance in many different diseases. In general, the tongue should be investigated, top and bottom, with reference to its color, dryness and size, palpated for lesions, and tested for its mobility Occasionally a worthy bit of diagnostic information will thus be perceived concerning the physical status of the tongue itself.

The mucous membrane which covers the tongue is modified skin Over the dorsal surface of the tongue are papillae. The filiform papillae are the smallest and cover the anterior two thirds of the tongue The fungiform papillae are larger and are scattered on the dorsum, sides and tip of the tongue and are set among the filiform papillae. The circumvallate papillae, seven to twelve in number, form an anteriorly curved row at the base of the tongue. In the median line, posterior to the curved row of circumvallate papillae, is the foramen cecum, which is the upper extremity of the remains of the thyroglossal duct. It is sometimes patulous for a short distance

On the posterior portion of the tongue, behind the circumvallate papillae, on each side of the median line, is a mass of adenoid tissue which forms the lingual tonsil

In the middle of the dorsum of the tongue is a furrow, caused by the septum binding the middle of the tongue down and allowing the muscles to rise on each side.

Anomalies. Reduction or absence of the tongue, referable to developmental arrest, and bifid and trifid tips, through persistence of the unfused apical components, are recorded

The commonest of all deformities of the tongue observed soon after birth is tongue tie, a fixation of the tip of the tongue to the floor of the mouth by a frenum which is too short When the fixation is extreme, the infant may not be able to nurse until the frenum is cut enough to loosen the tip of the tongue

Color and Pigmentation. The color of the tongue, as distinguished from the color of its coating, is of some diagnostic value The most frequent abnormal coloration of the tongue results from either food or drink The tongue is pallid in anemia and bluish in cyanosis A bright red tongue may be due to the exanthems, particularly in the early stage of scarlet fever, or to inflammation of the tongue itself (glossitis), it differs from the darker, reddened tongue of the deficiency states Petechiae, ecchymoses and infarcts may be found on the tongue, where they have the same significance as if found elsewhere Dark purple or blackish deposits of pigment may indicate an admixture of racial characteristics, or an old glossitis, or may constitute the discolorations of Addison's disease In jaundice the tongue is yellowish, with the yellow tinge particularly marked on the under surface of the tip. A series of clearly outlined yellowish white spots along the edges of the tongue is characteristic of xanthelasma

Uniform discolorations of the tongue and its coating may be caused by the ingestion of various substances, corrosive or noncorrosive Ammonia, bichloride of mercury, and sulfuric, carbolic and oxalic acids whiten the tongue, hydrochloric, nitric and chromic acids produce a yellow color. Potassium and sodium hydroxide redden the tongue Among the noncorrosive drugs and foods, bismuth, charcoal and iron stain the tongue black, wine, fruits and berries color it red or purple; and rhubarb, tincture of opium, tobacco, licorice and chocolate stain it brown or black.

Cross estimated that discoloration of the tongue constitutes at least 30 per cent of all oral reactions in patients taking penicillin orally. The discoloration appears as

ease is caused by invasion of a mixed infection, primarily represented by *Fusobacterium plauti-vincentii* in association with *Borrelia vincentii* At the onset the patient is aware of an uncomfortable feeling and salivation, and the tips of one or more of the interdental papillae on the buccal surface begin to swell They assume a livid, grayish color and become the sites of small, flat, punched-out ulcers that undergo necrosis The necrosis may destroy the gingivae down to the alveolar process. A strip of brown colored membrane may cover the affected gingival margin Removal of the membrane leaves a bleeding surface. The inflammation spreads rapidly, but only in severe cases is the palatal surface of the gingivae affected Contact ulcers form on mucous membranes of the cheek or on the borders of the tongue The disease may spread posteriorly to the tonsils The mandibular lymph nodes are painful and enlarged There may be fever, the temperature up to 104 F (40 C) The sense of taste may temporarily be completely lost

Trench mouth must be differentiated from avitaminosis, scurvy, pellagra and blood dyscrasias such as leukemia. Although there may be extensive and widespread destruction of the gum margins, the prognosis in trench mouth is good

Pyorrhea Alveolaris. There is no known systemic disease that will cause pyorrhea alveolaris, but there are two factors that produce the condition. an abnormal occlusal stress on the articulating tissue of the infected teeth, and coexisting disease that lowers the vitality of this articulating tissue. Pyorrhea alveolaris always presents deep pockets containing suppurating granulation tissue with, sooner or later, loosening of the teeth The patient usually presents himself for general examination to find the cause of receding gums In the aged the periodontium often is smooth and atrophied This atrophy, however, may occur at an early age; the condition should not be mistaken for pyorrhea alveolaris.

Abnormalities and Tumors. ***Hypertrophy.*** This is a slowly developing process, and usually a great amount of deformity is present before the patient is aware that the gums actually are getting larger There are, by the time awareness is aroused, a nodulated enlargement of the gums and an irregular arrangement of the teeth On palpation the nodulations are densely hard The mucous membrane is not affected

Diffuse Fibromatosis of the Gingivae. Diffuse fibromatosis of the gingivae may be hereditary No symptoms may occur until the fibromas become malignant and cover both sides of the alveolar processes of both jaws and even cover the crowns of the teeth By this time the teeth themselves may be crowded out of position The surface of the fibroma is light pink and is often roughened by papules and ridges of proliferative gum tissue The tumors often are large enough to distort the facial contour.

Epulis. An epulis is a fibrous tumor of the gum An epulis on the lower jaw is small and of slow growth An epulis of the upper jaw adjacent to a molar tooth or a bicuspid tooth is usually large when first seen The surface of the tumor has the color of the adjacent mucous membrane The mucosa is usually continuous over the surface of the tumor Occasionally epulides are bluish red and vascular in appearance Epulis recurring after one or two removals may become malignant

Granulomas of the Alveolar Borders. Dental granulomas develop from sites of irritation and are the result of infection. The usual history is that the granuloma or tumor has developed within recent weeks, within one or two months at the most The tooth on which the granulomatous tissue forms may be free of disease, but usually the deposits on its surface irritate the adjacent gum

These lesions begin as soft growths of the gum adjacent to a tooth or several teeth. If one tooth is involved, the granuloma usually is not a large one As these tumors grow older, they become harder and are usually less red than the surrounding tissue. Removal of the tooth, unless the granulomatous tissue also is removed,

plies the muscles which fix and depress the hyoid bone in chewing and swallowing.

If the cortical connections of the nucleus are involved, there will be paralysis but no atrophy; or if atrophy is present, it is slight. Contraction of the tongue due to the absorption, under treatment, of a lingual gumma may appear somewhat like paralytic atrophy.

Spasm. Spasm of the tongue is a rare symptom It may be tonic, in which case the tongue is contracted and rigid, or clonic, in which case the tongue jerks and twitches irregularly or is protruded and retracted rapidly. The movements usually involve both halves of the tongue, but may be unilateral

When clonic spasm of the tongue exists, it usually is a part or symptom of chorea, hysteria or epileptic convulsions, or is associated with mimic tic. Stuttering is a spasmodic affection of the lingual muscles. A curious disorder reported in those who use the voice incessantly, for example solo singers, is a spasm of the tongue on attempting to speak, a condition analogous to writer's cramp. Lingual clonic spasm is an occasional symptom in disseminated sclerosis and general paralysis Reflex irritation of the fifth nerve has been held responsible for lingual spasm and, in some instances, disease of the central nervous system produces it.

Tonic spasm of the tongue is indicative of hysteria or reflex irritation through the fifth nerve, occurring in nervously weak and debilitated persons. It may coexist with tonic spasm of other voluntary muscles

Tremor. A coarse tremor or trembling of the tongue is most frequently symptomatic of chronic alcoholism and is present in delirium tremens, it usually is present in brominism, and it may exist as a part of paralysis agitans A fibrillary tremor or fine twitching of the muscular bundles of the tongue may be seen in disseminated sclerosis, in general paralysis, and in bulbar paralysis when the lingual muscles begin to atrophy The tongue trembles in neurotic persons, particularly when they are excited or agitated.

Paralysis. If one side of the root of the tongue is higher than the other, and if when the tongue is protruded it deviates toward the same side, unilateral lingual paralysis exists There are likely to be some interference with speech and a slight difficulty in chewing and swallowing. If the tongue lies motionless in the floor of the mouth, the patient being unable to protrude it, and the functions of speech, mastication and deglutition are greatly impaired, there is total lingual paralysis. In both cases there may or may not be atrophy and fibrillary twitching. The absence of atrophy indicates a cortical or supranuclear lesion; the presence of atrophy indicates a nuclear or infranuclear lesion

Lingual paralysis, with atrophy of either one or both sides of the tongue, according to the situation or extent of the lesion, may exist as a symptom of the following conditions. general paralysis, chronic lead poisoning, embolism or thrombosis of the vascular supply of the basal nuclei, basal meningitis or tumor of the base, syphilitic disease or other disease of the bone at the base of the skull or of the first cervical vertebra, tumor of the upper portion of the spinal cord, and wounds of the neck

Inflammations. Inflammations of the tongue are likely to be diffuse. Their cause often is obscure. Lingual inflammations are characterized by pain, burning and swelling These symptoms may remain for days and gradually subside without leaving a trace. On examination the tongue is red and thick, the thickening being evident on palpation The increased heat of the tongue is readily discernible by the palpating fingers If abscess formation has occurred, a fluctuant region may be located on palpation

The tongue may appear enlarged when the floor of the mouth becomes inflamed Examination reveals edema under the tongue or under the chin Suppuration with abscess formation may follow.

early as 2 days, as late as 9 days and on an average of 4 days following the use of penicillin.

The Black Hairy Tongue. Black hairy tongue is an uncommon disorder and its cause is unknown It is thought in some instances to be due to a congenital abnormality which develops in later life. *It is a pigmentation and involves principally* the back of the tongue, the central furrow and portions of the pads, leaving the sides and tip unaffected. The color varies from yellowish brown to black.

Histologically, the filiform papillae are hypertrophic and hyperkeratotic and are the origin of hairlike filaments that may grow as long as ½ inch (1.27 cm.). The papillae become densely matted, and deposition of pigment takes place. The pigment is considered to be derived from food, wines, tobacco, iron and mercury, and mouth washes that contain oxidizing or reducing chemicals (Wolfson)

Black tongue has also been caused by the filamentous mycelia of actinomycosis which have been cultured from the tongue.

Dryness. The term appearance used with reference to the tongue usually relates to the character of the coating which may be present or to the disappearance of the coating and, particularly, to its degree of moisture The coating consists of accumulated epithelium, microorganisms and food detritus. Dryness of the tongue, when not caused by mouth breathing or coma, is of very considerable importance as an indication of general dehydration and prostration.

A thin, white, even furring of the tongue is normal in many healthy persons, *particularly those who are in the habit of smoking or of drinking milk*, and in mouth breathers. Such a coating is always present in moderately febrile states.

A tongue covered with a white fur through which project greatly swollen and bright red fungiform papillae is seen most frequently in acute infections, either generalized or limited to the tongue. This is not necessarily pathognomonic of scarlet fever

Size. Great enlargement of the tongue is easily determined. A slight increase in size can be assumed to be present if the edges of the tongue are indented by the teeth, the indentations existing only if the tongue is swollen beyond its normal limits

Macroglossia. This is a rare lesion of obscure origin Usually in such cases an abnormally enlarged tongue is observed in a child soon after birth A tongue of this type seems to grow slowly, and the whole organ is involved in the processes of enlargement. The tongue is firmer on palpation than the normal tongue. It may become so greatly enlarged that it lacks the capacity to move, and there may be local ulcerations where it has rubbed against or hung over the teeth

Enlargement of the tongue and a feeling of stiffness in it may accompany a general or regional amyloidosis Enlargement of the tongue occurs in acromegaly and in myxedema If associated with inflammatory symptoms, *the enlargement is* due to acute glossitis. If associated with urticaria or angioneurotic edema, it is allergic in origin Tumors of the tongue also are responsible for an irregular and sometimes great increase in its size.

Shrinking or Atrophy. The tongue is small after a profuse hemorrhage and may become noticeably lessened in size during starvation

In atrophy of the tongue, a condition which is due to some affection of the hypoglossal or motor nerve of the tongue involving its nucleus or its peripheral portion, the mucous membrane of the tongue is thrown into folds and the organ has [illegible] The atrophy is always conjoined with paralysis, and the [illegible] both lateral halves of the tongue accordingly as [illegible] Unilateral atrophy of the tongue sometimes is associated with facial hemiatrophy. Unilateral hypertrophy of the tongue sometimes occurs in congenital hemihypertrophy.

Spasm, Tremor and Paralysis. The motor supply of the muscles of the tongue is for the most part derived from the hypoglossal nerve. The same nerve also sup-

or both sides of the neck may become involved from a malignant growth in any portion of the tongue. Lymph nodal involvement is not always palpable.

The diagnosis is made on the basis of the histologic structure of biopsy tissue. The prognosis is usually unfavorable.

THE FLOOR OF THE MOUTH

On turning up the tip of the tongue a fold of membrane, the frenum linguae, is seen extending from the under surface of the tongue to the floor of the mouth beneath. In newborn children this fold of mucous membrane appears sometimes to be too short, hence the term tongue-tied. This anomaly may persist throughout life if not properly treated.

Between the teeth and the tongue, parallel to the alveolar process, is the sublingual ridge, formed by the sublingual salivary gland. On the median side of the sublingual gland are the lingual nerve and the submaxillary duct (Wharton's duct), and on each side of the frenum, on the anterior aspect of the sublingual ridge, is a papilla into which the duct opens Opening into the submaxillary duct, or by a separate duct into the same papilla, is the duct of the sublingual gland (the duct of Bartholin)

The Submaxillary and the Sublingual Salivary Glands. These glands present infections and tumors almost identical with those observed in the parotid glands. The submaxillary glands, like the parotids, may be absent or displaced, or there may be accessory glands

Infections and Inflammations. These disorders of the sublingual and the submaxillary salivary glands are not unusual occurrences The glands may be swollen during an epidemic of parotitis, but commonly they are affected in fevers and in serious illnesses much as the parotid glands are affected. Occasionally there is a low-grade inflammation of the sublingual and submaxillary glands which causes swelling of the ducts and obstruction to the flow of saliva during a meal Soon after eating, the patient becomes aware of a swelling under the chin along the inside part of the lower jaw. A swelling of this type may be painful, but it usually subsides within a few hours; it may not recur, or it may become rather annoying and recur at frequent intervals The swelling is due to obstruction of the duct by a tenacious secretion and subsequent edema and pressure.

Stones. Formation of sialoliths in the submaxillary ducts and the sublingual ducts is much commoner than in the parotid ducts

Salivary calculi usually originate within the gland structure in the form of small concretions which are carried along with the salivary current to become lodged in the gland duct. Here they become enlarged by deposits of bacteria and phosphates. Any of the salivary glands or ducts may be the site of calculous formations, but the most frequent location is Wharton's duct, after which, in order of frequency, the submaxillary glands, the parotid glands and Stensen's ducts.

The symptoms depend on the size and situation of the stone. If it lies within the gland structure, the patient may experience only a mild intermittent feeling of irritation and discomfort in the affected region together with moderate swelling If, however, the stone is in the duct, the symptoms may be severe, characterized by a sudden sharp pain when the salivary flow is stimulated and rapid, and painful distention of the gland In the course of 12 to 48 hours an inflammatory reaction may occur, due to the retention of infected secretions. General malaise may ensue.

The floor of the mouth may be dry, and frequently no saliva will be found flowing from the obstructed duct when the patient is asked to suck a piece of lemon. Palpation of the duct may express pus or reveal the location of the stone. Pus may be found in the floor of the mouth, together with swelling of the tissues along the course of the duct with deviation of the protruded tongue when the submaxillary gland is involved A probe passed into a salivary duct may fail to locate the stone If the calculus is large enough to cause obstruction, and particularly when it con-

Eczema. Eczema of the tongue gives rise to a condition variously known as *geographic tongue*, annulus migrans or wandering rash Ring-shaped patches, red and denuded of epithelium, are seen on the tongue, and under observation are seen to spread at the edges while healing at the center, coalescing and forming irregular areas with curved outlines Usually there is little or no discomfort from this condition

Scars, Fissures and Ulcers. Scars. Scars on the tongue may be the result of healed ulcers, of chewing the tongue during attacks of epilepsy or bulbar palsy, of accidental biting of the tongue during restless sleep or in careless chewing of food, or of a fall when the tongue is between the teeth.

Fissures. Fissures of the tongue, aside from the normal median longitudinal one, also are often of normal occurrence, especially in elderly persons. Deep fissures of the tongue are seen in Mongolian idiots. In other subjects fissures are often significant of chronic glossitis. Very deep inflamed fissures are often due to glossitis, and in an occasional instance are of syphilitic origin. Fissures or losses of substance at the edges of the tongue are usually due to deficiency states or to rough or broken teeth

Leukoplakia lingualis (ichthyosis linguae, leukoma, leukokeratosis, buccal psoriasis) is manifested by slightly elevated, thickened patches of irregular shape, not ulcerated, white and smooth on palpation, which sometimes show a tendency to fissure. They may furnish, in 1 case in 10, the starting point of an epithelioma

Ulcers. Acute and painful ulcers of the tongue are often due to aphthous stomatitis, less often to the ulcerative form of stomatitis. In chronic superficial glossitis shallow, red, glazed, denuded areas occur on the surface of the tongue. Multiple ulcers, gray, indolent, stellate, and associated with enlarged cervical lymph nodes, may be tuberculous and are almost always secondary to tuberculous disease of the lungs. Somewhat similar multiple ulcers may be syphilitic, but in such cases the anterior cervical lymph nodes are rarely enlarged Multiple small ulcers, preceded by vesicles, occur in smallpox, varicella, measles and erysipelas, as well as in pemphigus, herpes and eczema of the tongue

A single lingual ulcer with a hard base, associated with enlarged cervical lymph nodes, may be either the initial lesion of syphilis or an epithelioma When syphilis exists, the age of the patient is usually less than 40 years. The lesion is on the tip of the tongue, is not very painful and improves under treatment A mucous patch may become ulcerated, or a gumma of the tongue may break down, forming a deep sore A single ulcer, if opposite a rough or jagged tooth, may be simply the result of continued trauma, but the presence of an irritating tooth does not exclude epithelioma or syphilis

An *ulcer* on the *frenum linguae* may occur during the course of severe coughs, such as pertussis, from the thrusting of the undersurface of the tongue against the lower incisors habitually or during paroxysms of coughing.

Tumors. Benign Lingual Tumors. Any kind of benign tumor of the tongue is uncommon in adults Papillomas, small in size, are the commonest of the benign tumors. Fibromas, cysts, lipomas and hemangiomas may be encountered.

Malignant Lingual Tumors. Carcinoma of the tongue is commoner in men than in women, and commoner in middle-aged men than in either the young or the old.

Carcinoma of the tongue begins on the surface of the tongue either by a change in the epithelial covering or in fissures or ulcers at its edges. Some carcinomas of the tongue begin in leukoplakial spots, a few begin as benign papillomas, and still a few more begin in ulcers caused by broken teeth or defective dental structures. A greater number, however, just begin as sore places and continue as enlarging ulcers.

The lymphatic vessels from the mucous membrane and deep tissues of the tongue have apparently only a single outlet, so that the lymph nodes on either side

fluids through the nose on attempting to swallow, and if there is failure to pronounce correctly certain sounds; for example, the patient says "beng" for "beg." Inspection of the soft palate during the utterance of the long "ah" sound will show under normal circumstances that both sides of the palate arch upward. If the whole palate remains motionless during phonation of "ah," there is bilateral paralysis; if but one side moves, paralysis is unilateral.

Paralysis of the soft palate is most commonly due to diphtheritic neuritis or poliomyelitis, but is also caused by bulbar paralysis, brain tumors, basal meningitis and vertebral caries.

Anesthesia of the Palate and the Fifth Cranial Nerve. *Anesthesia* of the hard and soft palates indicates disease involving the second division of the *fifth nerve*.

The motor portion of the trigeminus supplies the muscles of mastication, namely, the two pterygoids, the temporal, masseter, mylohyoid, and anterior belly of the digastric

The sensory portion of the trigeminus affords sensation to the face, conjunctivae, nose, frontal and maxillary sinuses, teeth, palate, tongue, part of upper pharynx, external auditory meatus, and the scalp as far back as the vertex. It may or may not supply the sense of taste on the anterior two thirds of the tongue.

The motor functions of the trigeminus are tested by having the patient clench the teeth firmly, while the temporal and masseter muscles are palpated in order to observe their contraction. Also have the patient open his mouth. If the muscles on one side fail to contract, and the opened jaw deviates toward the paralyzed side, there is unilateral paralysis due to disease affecting at least the motor fibers of the inferior maxillary division of the trigeminus. Spasm of these muscles constitutes trismus or lockjaw

The sensory functions of the trigeminus are examined in the ordinary manner Whether one or all of its divisions are involved may be determined by comparing the areas of anesthesia found with its distribution If there is complete unilateral anesthesia, the patient when drinking can feel the contact of the cup or glass on one side only, affording a sensation as if half the vessel were missing. The sense of taste is partly conducted through the medium of the trigeminus There are certain inflammatory (herpes zoster), vasomotor (flushing, pallor), and secretory (lacrimation, salivation) disturbances which may arise from disease of the trigeminus because of the fact that it supplies the lacrimal and salivary glands with secretory fibers and is also the channel by which vasomotor fibers run The trigeminal nerve is involved in neuralgias and migraine. Trigeminal anesthesia is seen in hysteria, and in various forms of organic disease which, to a greater or lesser extent, involve the cranial nerves or the cranial nerve centers. Areas of cutaneous anesthesias, when the cutaneous nerves of the head and face are involved, are shown in Figure 4-1

Tumors. Slowly developing tumors of the palate are exostoses and ecchondromas They are situated in the midline, grow very slowly, and cause no trouble except that the patient is conscious of their presence The appearance of the tumors is characteristic They feel smooth and hard unless they are myxomatous or malignant.

THE FAUCIAL TONSILS

The tonsils are oval, and when normal in size, project but little if at all beyond the pillars of the fauces. They contain several recesses or crypts formed by the folding inward of the mucous membrane The walls of the crypts contain lymphoid tissue and mucous glands Extending from these crypts are pockets known as follicles These follicles may become sealed from inflammation which leaves palpably hardened areas in the tonsils

Acute Tonsillitis. Tonsillitis is most frequently met with between the ages of 10 and 30 years. The disease sometimes occurs in children less than 10 years of age and in adults of more than 50 years of age Tonsillitis accompanies many acute

tains calcium salts as its chief constituent, it is usually demonstrable in a roen genogram

Cysts. The term ranula generally is applied to any cyst in the floor of the mou that is due to obstruction of a duct of either a mucous gland or a salivary gland. Th cysts arise just behind the lower incisor teeth and may be due to involvement the incisor gland (glandula incisiva), but most commonly they are due to obstru tion of the excretory ducts of the sublingual glands. Among ranulas have been i cluded retention cysts as well as congenital inclusion cysts. Ranulas must be di tinguished from dermoid cysts The dermoid cyst has a thicker feel, more firm c palpation, and it often pits on pressure.

Tumors. Submaxillary tumors begin as small swellings beneath and medial t the border of the jaw just in front of the angle of the jaw. As a tumor of this typ becomes larger, it may occupy a considerable region of the neck. It is impossible t tell whether the growth springs from the submaxillary gland or the sublingual glan until the affected gland is identified

One of the common tumors of the submaxillary gland, as of the parotid glanc is the mixed tumor. The hard but elastic feel of these growths is characteristic. Th tumor is easily palpated by one finger of one hand on the floor of the mouth, wit the other hand under the chin. If the tumor has become malignant, it is fixed mor closely in its position

Carcinoma of the Floor of the Mouth. This lesion usually is an ulcer witl hard borders It often is found accidentally before it gives the patient any symptoms Some growths of this type are small rounded masses circumscribed and somewha movable, large tumors may form, however, filling the whole floor of the mouth an bulging into the neck

THE PALATE

The superior and lateral boundaries of the oral cavity and the differentiation of th nasal and oral cavities are the result of fusion of the two lateral maxillary processes o the first branchial cleft and the medial frontonasal process which descends from th anterior part of the head in the embryo Failure of fusion of these processes, in part o entirely, in embryonic life results in one or another variety of cleft palate *Cleft palat is discussed with cleft lip*

The anterior and posterior arches of the palate and the uvula are plainly visible The anterior pillar extends from the soft palate to the tongue and is formed by the palatoglossus muscle. The posterior pillar extends from the soft palate downward to the sides of the pharynx and is formed by the palatopharyngeus muscle In front of these arches, and extending from the roof of the mouth opposite the posterior edge of the last molar tooth downward to the posterior edge of the alveolar process of the lower jaw, is an elevation of the mucous membrane which shows the line of junction of the hard and soft palates

Torus palatinus is a protuberance of the hard palate at the line of closure of the maxillary sutures These swellings are unimportant clinically They are often of concern to the patient.

The anterior three fourths of the roof of the mouth is formed by the hard palate and the posterior one fourth by the soft palate

Vesicles arranged in annular shape on the soft palate or perhaps on the pharyngeal wall, and attended with a disproportionate amount of pain, are viral herpes of the same sort that occurs elsewhere on the mucous membranes of the mouth When these vesicles rupture, small ulcerations follow and constitute the commonest acute ulcerations of the palate Chronic ulcers of the palate are often of syphilitic origin.

Perforation of the soft palate or its *adhesion*, either partial or complete, to the posterior pharyngeal wall, may be the result of any severe infection or due to syphilitic ulceration or diphtheria

Bilateral paralysis of the soft palate is to be suspected if there is regurgitation of

portion of the membrane or of a swab from the surface of the tonsils. The presence of Klebs-Löffler bacillus (*Corynebacterium diphtheriae*), when culture is made on the proper media, indicates diphtheria

In regard to the relationship of acute tonsillitis and scarlet fever, see Streptococcal Infections in Chapter 17.

In cases of uncomplicated tonsillitis the outlook is always favorable. The disease runs its course in about a week. Peritonsillar abscesses or quinsy may occur and when they do develop, they greatly increase the discomfort of the patient. In peritonsillar abscess or quinsy the prognosis is more guarded, especially because of the possibility that the more virulent infection may produce septicemia or Ludwig's angina.

Corynebacterium diphtheriae (Klebs-Löffler Bacillus) and Diphtheria. The causative organism of diphtheria is of the order Eubacteriales Buchanan, family Corynebacteriaceae Lehmann and Neumann, genus *Corynebacterium* Lehmann and Neumann, and species *Corynebacterium diphtheriae*.

The optimism that prevailed during the first three decades of the twentieth century with regard to the successful therapeutic control of diphtheria yielded to pessimism and perplexity when numerous instances of malignant diphtheria occurred in central Europe, for these cases were wholly refractory to routine methods of serum therapy Later the instances of *malignant diphtheria* proved to be a special type, due to *Corynebacterium diphtheriae gravis* Since this division was made, the name *Corynebacterium diphtheriae mitis* has been employed to designate the nonmalignant strain.

The extracts of the gravis strain produce necrotizing and edematous lesions resembling the local reactions to potent staphylococcal or streptococcal toxins The main product from gravis strains is an endotoxin analogous to the Duran-Reynals spreading factor formed by certain invasive strains of pyogenic cocci The severe lesions of malignant diphtheria are due to the synergic effects of classic diphtheria toxin with gravis endotoxin The gravis strains of diphtheria may account for the exceedingly large quantities of antitoxin required for the successful control of the symptoms in an occasional patient who has diphtheria.

There are conferred active immunity and passive immunity to diphtheria Active immunity now is conferred by the use of especially prepared toxoid solution, of which one injection produces immunity

The diphtheria organisms are transmitted by droplets, food, handling of articles in common use, such as toys, and by contact directly or indirectly through clothing The germs can live for weeks on toys and clothing and on various household utensils that are not in common use

The carrier rate increases with the beginning of cold weather. The presence, in the nose of a subject, of bacilli that appear morphologically to be those of diphtheria is not enough to justify giving the person the stigma of carrier and enforcing isolation for treatment The bacilli should be isolated and their virulence proved bacteriologically before the subject is labeled a diphtheria carrier and before isolation is advised

Susceptibility of the individual to diphtheria can be determined by tests If susceptibility exists, prophylactic treatment can be given that usually suffices for control.

Schick Reaction The blood of the majority of normal adults contains a small amount of diphtheria antitoxin, a fact which probably accounts for resistance of many persons to diphtheria The presence of the antitoxin may be easily detected by means of the Schick reaction A standardized diphtheria toxin is diluted in physiologic salt solution so that 0 1 ml of the solution contains 1/50 of the minimal lethal dose for a guinea pig This dose is injected intracutaneously If the blood of the subject tested has less than 1/30 unit of antitoxin per milliliter, a positive skin reaction appears in from 24 to 36 hours and persists for 4 or 5 days or more. A positive reaction consists in a slight infiltration of the skin surrounded by a red areola 1 to 2 cm in diameter. Positive reaction indicates susceptibility, negative reaction indicates natural immunity to diphtheria. The naturally immune person, however, may harbor the bacilli and be a carrier; it follows, therefore, that many carriers may give negative reaction

Negative reactions to the Schick test are obtained in 9 out of 10 of the newborn, but become less frequent in children up to the second to the fifth year As children grow

illnesses. It is present in the initial stage of measles and scarlet fever. It is frequently present in diphtheria and in secondary syphilis. Water and milk may carry infective organisms for tonsillitis Tonsillitis is sometimes infectious and not infrequently epidemic Hemolytic streptococci, often in pure culture, have been found during epidemics of acute tonsillitis in military camps and in civilian practice. The diplococcus of pneumonia is said to be responsible for less than 10 per cent of cases of acute tonsillitis, and to the *Hemophilus influenzae* organism (bacillus of Friedlander, *Klebsiella pneumoniae*) is attributed a very large percentage of benign membranous tonsillitis

If the tonsillitis is limited to the catarrhal variety, the surface of the tonsils shows the changes common to inflammation of the mucous membrane. In other cases, the so-called lacunar variety, the morbid changes are confined mainly to the crypts In the so-called parenchymatous tonsillitis there is congestion of the whole tonsil

SYMPTOMS. An attack of tonsillitis is not necessarily ushered in with symptoms referable to the throat. There may be such symptoms as fever, sometimes chills and fever, the temperature reaching 102 to 103 F (38 9 to 39.4 C) and in severe infections as high as 105 F (40 6 C) In most instances of tonsillitis the local symptoms make themselves felt at once The illness begins with a feeling of fullness in the face and the throat, amounting soon to sharp pain which extends up to the ear and is generally augmented on attempt to swallow There may be so much pain on trying to swallow that the patient quits eating and drinking. The voice becomes thick and muffled, the senses of smell and taste are suspended, and there may be deafness from eustachian catarrh. Headaches, backaches and pains in the arms and legs are of common occurrence

EXAMINATION. The lymph nodes at the angle of the lower jaw are swollen and in most cases are very tender, so that the head is held stiffly The throat is often difficult to examine in those who have acute tonsillitis, for the pain is intense when they try to open the mouth, and consequently a view of the back of the throat is often facilitated by the use of a head mirror The inflammatory process extends to the anterior faucial pillars, the uvula, soft palate and pharynx, where the evidence of pharyngitis may also be apparent The congested surface of the tonsils is often spread over irregularly with debris which occludes the orifices of the tonsillar crypts This debris may accumulate and as time passes may form a white, grayish or dirty yellow membrane This membrane, in contrast to that accompanying diphtheria, is readily separated from the tonsil and does not leave a bleeding surface when it is removed The swelling produces obstruction of the circulation in the region of the tonsil and leads to edema in the more relaxed tissues on the posterior wall of the soft palate, which may be seen hanging down in a translucent bag on each side of the uvula The soft palate may become so impeded in its action that the voice becomes almost unintelligible, and the attempt to swallow liquids may be followed by regurgitation through the nostrils

Tonsillar abscesses are rare, but when they do appear they discharge their purulent contents into the pharynx without ill effects

DIAGNOSIS. The diagnosis generally presents no difficulty. Acute follicular tonsillitis must be differentiated from diphtheria. Diphtheria generally is more gradual in its onset and it is more likely to begin on one side, or at least it does not start on one side and then develop on the other, as does tonsillitis There are less pain and fever in diphtheria. The mouth is opened more easily and the throat, with the characteristic adherent, spreading, false membrane, may be viewed more easily in diphtheria than in follicular tonsillitis. The false membrane in diphtheria generally invades the soft palate and uvula and often spreads to the larynx, postnasal space and the nose The younger the patient, the more likely is the condition to be diphtheria. In doubtful cases the final diagnosis is to be made after culture of a small

whereas in others there is a chronic parenchymatous hyperplasia in which the tonsil is soft and friable, in still others there is a slow fibroid degeneration, an increase in the connective tissue stroma In tonsils with fibroid degeneration there may be cyst formation or the deposit of calcareous masses.

Of paramount importance is the fact that the size of the tonsil is not a criterion of an infectious disease. Some of the largest tonsils give rise to the least local inflammatory trouble, whereas small tonsils which have adhesions about their borders, and the remains of tonsils which have been imperfectly removed surgically may be the source of serious illness of the patient. The tonsil is more to be suspected as a septic focus when creamy pus can be expelled regularly from the fossa, or when a congested appearance of the tonsil suggests an infection in the follicles themselves which has cut off communication with the surface. Such conditions may be associated with permanent injection of the buccal surface of the anterior faucial pillar and sometimes with enlargement of the lymph node just behind the angle of the jaw. On neither clinical nor bacteriologic examination of the tonsils before operation can it be decided that a tonsil is a focus of general infection, even if hemolytic streptococci are obtained in pure culture from the tonsils. The decision in regard to focal infection can be made only after the tonsils have been removed and the patient has returned to good health The return of good health is presumptive evidence that the tonsils were a focus of infection.

Kaiser did not observe immediate benefits after the removal of tonsils in children, but over a 10-year period following the removal of tonsils there were a reduction in the incidence of sore throat, and a decrease in the susceptibility to scarlet fever, diphtheria, cervical adenitis, first attacks of rheumatic fever, and otitis media.

Symptoms. In some children and adults there are very definite symptoms from enlarged tonsils The tone of the voice frequently is thick, and there is a ring or resonance about it which can be distinguished from that caused by nasal or laryngeal obstruction Articulation may be indistinct. If the patient makes a complaint, it may be of a sensation of fullness in the throat. Often there is a recurring eustachian catarrh with each bad cold The cervical lymph nodes are chronically enlarged. There may be a foul breath or a disagreeable taste in the mouth

Hypertrophied tonsils which should be surgically removed are accompanied by a history of frequent attacks of tonsillar inflammation or of peritonsillar abscess. There is interference with respiration by day or by night, and occasionally an alteration of the voice is noticeable.

The prognosis after the removal of the tonsils in those who have had repeated attacks of eustachian catarrh or inflammatory disease of the middle ear is guarded. The removal of the tonsils in the presence of these diseases should be advised strictly on its own merits for treatment of the local condition which may be demonstrated. No doubt at times general systemic benefits will be obtained from the removal of the tonsils, but these benefits cannot be predicted.

Singers, or those who wish to be singers, often want to know if removal of the tonsils will interfere with singing In those who are already singers there is certainly a risk that the instinctive control of the muscles used in singing may be temporarily lost to such a degree as to impart a peculiar tone to the voice which previously was prized However, in those who are already singers, after tonsillectomy a renewed study and practice will often result in a stronger and better voice, if not one of precisely the same tone

Patients who are only beginning the study of singing can safely be advised to [illegible]

to relearn the complete use of the muscles which have been liberated by removal of the tonsils.

beyond the fifth year, negative reactions increase, and in adult persons the same ratio of negative to positive skin tests prevails as in newborn children; that is, 9 out of 10 are negative.

SYMPTOMS. The period of incubation of diphtheria varies from 2 to 10 days, but is usually 2 or 3 days The onset is with fever, temperature 102 to 104 F (38.9 to 40 C), chilliness, headache and pain in the back and limbs

There is nothing distinctive in the initial symptoms, which vary according to the site of the specific inflammation. Generally there are sore throat and dysphagia. A croupy cough, hoarseness or aphonia, and above all, evidences of progressive laryngeal stenosis constitute a dangerous involvement of the larynx If there is an extension of the membrane into the trachea and the bronchial tubes, the breathing may become stridulous, and dyspnea and cyanosis are manifest

Often the symptoms of diphtheria are mild, with slight fever and little if any prostration In diphtheria gravis there are extensive and intense local changes, the prostration is extreme, the temperature is subnormal, the face is ashy, the pulse rapid and feeble. Subcutaneous ecchymoses appear

Extraneous infections and symptoms of diphtheria are common A cutaneous wound may become infected and a pseudomembrane may form at the point of lodgment of the germs Diphtheria of the conjunctiva may occur primarily, or by extension from the nose; of the external ear, from the discharge of a diphtherial otitis media; of the mouth and lips, by extension; of wounds, ulcers, and the genitals, by direct infection from contaminated hands, instruments, or dressings. Diphtheritic paralysis may be a serious complication (see Chapter 15).

EXAMINATION. There are swollen and tender cervical lymph nodes. There may be apparent stiffness of the cervical tissues

The tonsils are swollen and covered with grayish or yellowish white membrane, which is usually adherent and leaves a bleeding surface when forcibly stripped off. By the second or third day the membrane extends to the faucial pillars, perhaps also to the uvula and the posterior pharyngeal wall Under favorable conditions the symptoms subside and the throat becomes clear of membrane by the tenth day

If the inflammation extends to the nose, there is an offensive, often bloody, discharge from the nostrils, or epistaxis. In certain instances, there may be thick membranes in the nose containing diphtheria bacilli, but constitutional symptoms are absent and the disease is relatively harmless (fibrinous rhinitis) On extension of the infection to the tonsils the membrane may appear punctate and be confined to the tonsils, simulating an ordinary follicular tonsillitis, or there may be a soft nonmembranous exudate on the tonsils alone; or the disease may be so extremely mild that membrane or exudate does not appear, the throat presenting only the redness of an ordinary catarrhal inflammation

On extension of the disease to the larynx the supraclavicular, episternal, intercostal and epigastric spaces are deeply retracted with inspiration and bulge with expiration. Shreds of membrane may be coughed up If the stenosis is not relieved, the child passes into a semicomatose state and death ensues after a few hours to several days.

DIAGNOSIS. The diagnosis is established by positive cultures from the throat for the Klebs-Löffler bacillus in the presence of a membrane and other variable symptoms and signs as enumerated.

Chronic Tonsillitis; Chronic Enlargement of the Tonsils. The cause of lymphoid hypertrophy of the tonsils is not known. Generally the tonsils begin to enlarge at the age of 3 or 4 years They begin to shrink at about the age of 12 years, and tend to diminish or to become much smaller at about the age of puberty. Sex does not seem to have any influence on occurrence of tonsillar hypertrophy. In a hypertrophied or an enlarged tonsil there is an increase in the normal structures. In some the crypts are more distinctive and contain a variable amount of mucus,

unilateral enlargement or a deep, spreading ulceration on an enlarged tonsil, from which an offensive, sanguineous discharge issues, is in all probability cancerous.

Most malignant tumors of the tonsils are anaplastic epidermoid carcinomas arising in the mucous membrane covering the tonsil or lining a crypt Lymphosarcoma of the tonsils arises less frequently. The malignant lesions arising within the tonsil itself are usually more rapidly growing and much more radiosensitive than are carcinomas arising on neighboring mucous membranes and invading the tonsil secondarily. The diagnosis is made by biopsy study of tissue secured from the lesion or of the removed tonsil.

THE NOSE

The nose is long, short, flat, small or large. The contour of the nose viewed in profile is formed by an upper portion of bone, the bridge of the nose; a middle, of cartilage, and a lower, or tip, also of cartilage. The bridge of the nose slopes downward and forward, and where it joins the upper lateral cartilage, the line changes and slopes more sharply downward until the tip is reached Here the lower lateral cartilages bulge forward, forming a rounded and often a projecting tip

The skin over the tip and alae is thick and adherent to the cartilages. It possesses a comparatively scanty blood supply, hence its liability to suffer from exposure to cold, and it is a favorable site for ulcerations (lupus) and superficial epithelioma (rodent ulcer). Sebaceous and sweat glands are abundant. The skin is often pockmarked from acne. Stiff hairs guard the inside of the nostrils. The follicles of these hairs are often the seat of small furuncles or boils which are extremely painful, owing to the tension caused by the congestion and the swelling, which is restricted by the tissues being so firmly bound to the cartilages beneath.

Anomalies and Deformities. A nose with stenosed nares or an incomplete septum represents a persistence of the normal fetal anatomy A failure of the region between the nasal sacs to consolidate into a septum permits apical bifurcation or duplication of the nose. A rare anomaly of the nose is cyclopia. a tubular proboscis attached above the single median eye

The nose may be long and its midportion bowed forward with the tip turned down toward the upper lip Such a deformity is of developmental origin, often hereditary Contrasted with the nose of this shape is the short nose with the external surface curved inward toward the face, with the nares large and pointing outwardly and very obvious. The shape of this nose too is of developmental origin, often hereditary A comparable deformity, less the forward opening of the nares, is produced by surgical injuries and traumatic fractures of the bony part of the nasal septum This deformity may be, but is rarely, due to syphilis The nasal septum may become ulcerated and perforated and deformed so severely from the inhalation of toxic gases that the external contour will become deformed

In cretinism and myxedema the nose becomes coarse and broad It is broadened or distorted and displaced by growing tumors in the nasal cavities or in the adjacent facial bones.

Rhinophyma and Redness. Rhinophyma is a chronic hypertrophy of the skin of the nose and edges of the alae nasi. The cause is rosacea, and the condition occurs in middle-aged or aging men

Chronic redness of the nose is due to dilated capillaries and, if not normal, it usually results from sunburn, windburn or rosacea It is rarely due to chronic alcoholism

Small dilated blood vessels appearing over the tip and alae of the nose occur in different disease conditions, especially cirrhosis of the liver In this disease the small nevi, vascular spiders, formed by small dilated vessels, which are known to be minute arteries, are a common although not a diagnostic manifestation The

Peritonsillar Abscess (Quinsy or Cynanche). Inflammation and formation of pus in the tissues adjoining, but outside, the tonsil is known as quinsy. The condition is a peritonsillar abscess

The illness begins with fever and a chill, which is followed by an acute pain behind the angle of the jaw and extending up to the ear and down the neck on the same side as the abscess. Swallowing is so painful that often the patient will allow the saliva to run from the open mouth rather than endure the pain that attends an attempt to swallow or to expectorate. Accumulation of secretions in the pharynx adds a rattling character to the heavy thick tone of the patient's voice The neck is held stiffly and the head is forward and inclined to the affected side. The tongue is protruded with the greatest of difficulty Thirst often is intense. Taste is lost early in the disease and the sense of smell is diminished. The patient's breath becomes offensive, and the patient is pale and anxious and soon is very much exhausted The temperature in the early stages of the disease may reach as high as 105 F (40 6 C) The abscess often ruptures through the tonsil itself into the superior tonsillar fossa or through the anterior pillar and soft palate. With rupture of the abscess, after 5 to 10 days, the general symptoms cease at once and the local discomfort abates rapidly. Some days or weeks are required before the patient returns to normal health

On examination there is tenderness over the whole side of the neck. The lymph nodes at the angle of the jaw and along the sternocleidomastoid muscle are swollen and tender. Diffuse tenderness also may be present in the submaxillary, parotid or occipital nodes. The isthmus of the fossae is considerably narrowed by the bulging of the anterior pillar and neighboring portion of the soft palate The swelling may be such that the tonsil itself, which may not actually be swollen at all, may not be visualized The surface of the tonsil and the abscess often is coated with a deposit of mucopus resembling a false membrane, which is readily detached. A valuable sign in the diagnosis of a peritonsillar abscess is a loss of mobility of the soft palate on the affected side The tip of the uvula tends to point toward the tonsil around which there is an abscess Edema of the larynx is rare but if it occurs, it may be of very serious import

A patient usually recovers from a peritonsillar abscess, but the spontaneous bursting of a large abscess which floods the trachea with pus while the patient is asleep may cause death. Hemorrhage from a peritonsillar abscess may occur as a primary or as a secondary event, with or without surgical drainage of the abscess

Among the possible complications of quinsy are septicemia, bronchopneumonia, thrombophlebitis, pyemia, cellulitis of the neck, seropurulent pleurisy, meningitis, suffocation from pressure, secondary edema of the glottis and acute edema of the lungs

Tuberculosis. In the adult, tonsillar tuberculosis is of slight importance because, on the whole, it is only a secondary localization in an advanced pulmonary tuberculosis In children, it presents as either a secondary localization to pulmonary tuberculosis or a form of pharyngeal infection Tonsillar tuberculosis may be latent and thus is detected only by histologic examination Tuberculosis of the cervical lymph nodes and tonsillar tuberculosis are frequently associated. Every patient whose tonsils disclose tuberculosis should be kept under observation until it is clear that pulmonary tuberculosis is not present Tonsillectomy involves no great risk in the presence of tonsillar tuberculosis if the pharynx too is not deeply involved.

Tumors. There is a general belief that simple tumors of the tonsils are practically nonexistent. This statement is generally true, however, papillomas, adenomas, fibromas, angiomas, dermoid tumors and, occasionally, lipomas are all seen in this region. In addition to these tumors occasional keratomas, mixed tumors and retention cysts and hardened areas of scar tissue are seen.

Malignant tumors of the tonsils occur after 50 years of age In an elderly person

Discharges From the Nose. Nasal discharges may be watery, mucous, mucopurulent or purulent; or bloody or composed of blood alone, according to the nature and seat of the causal condition.

A *watery discharge* marks the beginning of acute coryza, vasomotor rhinitis, hay fever, the catarrhal form of epidemic influenza, pertussis, measles, and typhus and other fevers. In a few days a watery discharge often grows thick and mucopurulent. Watery fluid may flow from one nostril during an attack of trigeminal neuralgia. An occasional watery discharge, with persistent obstruction of one or both nostrils, may be due to nasal polyps. A recurring flow of pus from one nostril, particularly if brought on by lying on or leaning over toward the side opposite to that which is discharging, is probably due to an antral abscess, and the probability is increased if bad teeth are present. In children the possibility of a foreign body should not be overlooked in all instances of nasal discharges not easily accounted for. Finally, irritating gases or powders will produce a smart watery flow

Bloody discharge may be significant of an impacted foreign body. Coming on in the course of pharyngeal diphtheria and irritating the parts with which it comes in contact, such a discharge may indicate nasal infection before membrane can be discovered in the nasal cavities. An offensive discharge from both nostrils, which may be accompanied with greenish gray crusts, is symptomatic of atrophic rhinitis, or may be due to syphilis, caries or necrosis of the bones. It may be a sequel of scarlatina. The patient is usually unconscious of the fetid odor. Cancer or lupus affecting the nasal chambers or encroaching on them may also be responsible for a discharge possessing an unpleasant smell

Cerebrospinal Rhinorrhea. This is a rare condition caused usually by operative or accidental trauma, especially fractures at the base of the skull. It may begin without any known cause. In instances of increased intracranial pressure spinal fluid may escape to the nose and in the presence of the accompanying disturbances of the sensorium and the recumbent position of the patient it drains back into the throat and causes gurgling, coughing and choking Ordinarily there is a constant drip of the clear fluid from the nose.

The diagnosis depends on the presence of a clear fluid from the nose which does not contain mucin or albumin but contains sugar as evidenced by the reduction of copper in a copper-containing solution such as Fehling's solution

Epistaxis. A discharge of blood from the nose may be a result of either local or general causes It is usually a capillary oozing, and on inspection the bleeding area is seen to be congested, ecchymotic or superficially ulcerated A common site of the bleeding spot is on the cartilaginous septum Less frequently it arises from the posterior end of the middle turbinated body or, in children with adenoids, from the vault of the pharynx or at times from the accessory sinuses Specular inspection under a good light, clots having [illegible]
termine the exact location of the [illegible]
the blood may run into the ph [illegible]
vomited or, if clinging to the pharynx, be hawked up, thus simulating hematemesis or hemoptysis Nosebleed from local causes is usually unilateral, but if the nosebleed is due to blood changes or general diseases, it is likely to take place from both sides.

Ordinarily epistaxis is not sufficiently severe to produce constitutional symptoms, but after trauma or operations on the nose or in cases of hemophilia it may be profuse or continue long enough to threaten life seriously, although an actual fatal result is extremely rare

Nasal Causes of Epistaxis Aside from traumatic causes, caries or necrosis of the nasal bones, ulceration from a foreign body or other causes, polyp, new growths, varicosities or chronic nasal catarrh may be responsible for epistaxis. Hypertension with accompanying arteriosclerosis and alcoholism may render the vessels liable to rupture. The latter causes rarely produce nosebleed.

General Causes of Epistaxis People of full habit may have a rather frequently recurring nosebleed Delicate children suffer from it, especially at puberty and after

vascular nature of the spiders may be demonstrated by pressing the point of a pencil on one of the arteries where it is seen to emerge from the deep layers of the skin. During application of pressure in this manner the vessel is obliterated.

Acute redness of the nose, with pain and swelling, especially of one ala, may be the result of a small pustule or boil.

In a young person a superficial ulceration of the wing of the nose, usually painless, beginning as a reddish papule, spreading in various directions, and healing in one portion while breaking down in another, is probably a tuberculous ulcer. In an elderly patient a small, hard, scabbing ulcer, somewhat painful, gradually extending, and perhaps attended with involvement of lymph nodes, is an epithelioma.

Collapse of the Alae Nasi. The alae nasi collapse when an unnatural weakness of the lateral aspects of the lateral walls of the distal part of the nose is present. This condition is a developmental defect, often inheritable. The nose is long and narrow in contour. The collapse of the nares occurs during inspiration and thus produces varying degrees of nasal obstruction.

Atresia of the Alae Nasi. In congenital atresia of the alae nasi there is a failure of perforation or absorption of epithelium of the developing nose. Acquired atresia of the alae may be engendered by healing tuberculosis, syphilis or trauma.

Acting Nares; Regurgitation of Fluids. In some sensitive and neurotic individuals the nostrils dilate with each inspiration, especially under mental excitement. Aside from this, acting nares indicate dyspnea or anoxia of various origins, and among other conditions are very noticeable in emphysema, asthma, pneumonia, obstructive diseases of the larynx and the broken compensation of cardiac valvular lesions.

If on the patient's attempting to swallow fluids a portion escapes through the nostrils, one of three conditions is usually present: cleft palate, paralysis of the soft palate (diphtheritic) or bulbar paralysis.

Pain in or Around the Nose. Burning or smarting sensations usually attend coryza or other acute catarrhal inflammation. If great pain in the nasal chambers is present, it may be a symptom of an ulcerating lesion or of an impacted foreign body. Severe pain just above the root of the nose, accompanied with fever, may be due to inflammation of the frontal sinuses. Pain in the nose and cheek is due to inflammation of the antrum. Pain referred to the nasal cavities and ears is due to inflammation of the eustachian tubes. Inflammation of the eustachian tubes is often associated with diseases of the nasal passages. A sensation of dryness is a common complaint in the early and late stages of coryza and is a persistent and annoying symptom of atrophic rhinitis.

Inflammation and engorgement of the turbinates, ostia, nasofrontal ducts and superior nasal spaces are responsible for most of the pain from most of the paranasal structures. The pain emanating from the nasal and the paranasal structures is relieved by shrinkage of the nasal structures.

Diseases of the superior nasal structures cause headaches, primarily in the front and top of the head and between the eyes. Diseases of the middle and inferior nasal structures cause headaches over the zygomas and temples and in the teeth and jaws.

When the turbinates are painful, the pain is augmented by shaking the head and by lowering it between the knees. The presence of purulent secretion in the sinuses is not necessarily the basis for headache.

Local vasomotor changes in the erectile tissues of the nose occur as accompaniments of stress, exhaustion, sexual excitement, and various emotional states which may or may not be associated with symptoms. If there should be inflammation of the nose, these changes enter awareness and thus cause symptoms. Furthermore, congestion of the nasal mucous membranes may occur without inflammation as an accompaniment of anxiety or resentment.

To test the function of the olfactory nerve, nonirritating substances must be used, as pungent vapors affect mainly the trigeminal nerve Suitable odorous agents are musk, oil of cloves and peppermint in convenient containers It should be remembered that the perception of any single odor is lost in 3 or 4 minutes but is regained after 1 minute of rest. It is essential that the odorous material should enter the nostrils as a vapor or in a state of fine division, the act of smelling is usually assisted by sniffing, which is a modified inspiration. It is also necessary that the mucous membrane should be moist in order for the odorous particles to enter into solution on its surface.

The clinical symptoms relating to the sense of smell are *anosmia*, loss of the sense of smell; *hyperosmia*, increased sensitiveness of the sense of smell, and *parosmia*, subjective perversion of the olfactory sense.

Anosmia. The loss of the sense of smell, in the majority of instances, is due to local disease of the nasal mucous membrane, namely, chronic rhinitis, particularly the atrophic variety, and polyps or other new growths. The inhalation of irritating vapors or extremely foul odors may temporarily or permanently abolish the sense of smell. Paralysis of the trigeminal nerve will impair the olfactory power of the affected side. Loss of the power of smell may be a symptom, purely neurotic, of neurasthenia and hysteria.

Frequently the sense of smell is abolished because of injury or lesion of the olfactory bulb or tract Falls or blows on the head, affecting the nerve in its course, may produce as the only symptom of injury a persistent anosmia. Caries of the bones supporting the tract or bulb, and basal meningitis or tumors involving the nerve, may be instrumental in causing olfactory anesthesia. Possibly from atrophy of the nerves, anosmia may be one of the symptoms of locomotor ataxia. Anosmia is sometimes congenital, resulting from imperfect development of the olfactory nerve tissue Partial anosmia may be due to a lesion of the uncinate gyrus or to disease of one hemisphere

Hyperosmia. Hyperosmia or abnormal sensitiveness of the sense of smell is, in its slighter degrees, not an uncommon symptom in neurotic individuals More rarely the sensitiveness is extreme and is symptomatic of hysteria and neurasthenia

Parosmia. Olfactory sensations without a physical basis, the apparent odors usually being unpleasant or offensive (*kakosmia*), are not infrequent as hallucinations in the psychoses A bad odor may constitute the premonitory aura of epilepsy Subjective kakosmia has been associated in a limited number of cases with tumor of the hippocampus

Olfactory Acuity and Appetite. Elsberg and Levy introduced a simple method of measuring olfactory acuity Measured volumes of odorous air were injected into both nostrils The smallest volume which produced a sensation of odor was taken as a measure of the olfactory threshold Using bottles containing constant amounts of ground coffee as sources of odorous air, Goetzel and associates measured the diurnal variations in olfactory acuity They found that on days when lunch was omitted the olfactory acuity increased gradually from the early morning until the end of the work day. This increased olfactory sense was accompanied with a parallel increase in the hunger sense This basic pattern was modified on days when lunch was eaten during the midday rest period As a result of the lunch the olfactory acuity fell precipitously to a relative olfactory insensitiveness as the sensation of hunger was converted into one of satiety This dullness of the olfactory sense persisted for about 3 hours, when a rapid increase in olfactory acuity set in, accompanied with a return of the hunger sense

Postnasal Drip. A postnasal drip is of importance mainly from the local discomfort and anxiety that it gives the patient who is thus affected

Postnasal drip is produced by many and varied etiologic agents It is often associated with the various forms of rhinitis, lymphoid hyperplasia of the pharynx, and enlarged adenoids and lingual tonsils It is caused by irritations and by dust on the nasal mucous membranes, as well as by excessive tobacco smoking and medications in the way of nasal sprays and nasal washes containing drying agents. The

exertion under a hot sun. It is a common complaint of mountain climbers at considerable altitudes, and inhalation of very hot or very cold air may induce it. In suppressed menstruation it may be vicarious The chronic anemias are frequently attended by epistaxis It is a symptom of leukemia, purpura haemorrhagica and scurvy and is the most ordinary form of hemorrhage in hemophilia. Less commonly it may be the result of cardiac hypertrophy and valvular disease, enlarged bronchial lymph nodes, pleurisy with large effusion, emphysema and the strain of pertussis.

Epistaxis is a symptom of diagnostic value in the prodromal stage of typhoid fever, and is an occasional event in other infections such as erysipelas, pyemias, malarial fever, viral, rickettsial and leptospiral infections

[illegible] Telangiectasia (Osler's Disease). This telangiec- [illegible] by the presence of multiple acquired angiomas of varying [illegible] with a tendency to bleed spontaneously or from slight trauma The disease has been traced through six generations in one family In about 20 per cent of the cases there is no family history of a simi- [illegible]

[illegible] ectasia of preexisting vascular channels [illegible] endothelial [illegible] taxis

[illegible] develop in the [illegible] treatment, the lesions have a universal [illegible] a tendency to disappear spontaneously while new angiomas appear

The first symptom is abnormally profuse epistaxis beginning at about puberty. This is followed by the development of multiple telangiectasias of the skin and mucous mebranes from the age of 25 to 35 years All symptoms tend to reach their greatest severity from 30 to 39 years of age

Fissure on the Nasal Vestibule. A fissure on the nasal vestibule is a common complication or sequence of a nasal discharge from any cause. It often happens during the course of coryza and hay fever. A less common cause is syphilis The fissure is painful and the tip of the nose is tender The skin about the fissure is reddened

Sneezing. This is a spasmodic expiration, caused usually by direct, rarely by reflex, irritation of the sensory nerves of the nose, which occurs as an early symptom of coryza, measles, pertussis, asthma and hay fever Small doses of the iodides in susceptible individuals, and large doses in many others, will induce it, as well as the inhalation of various irritants such as dust, pepper and snuff Prolonged paroxysms of sneezing have been asserted to be of hysterical origin Syringing or manipulation of the external auditory canal will sometimes provoke a reflex sneeze A common cause of sneezing is a hypersensitive lining of the nose such as is present in vasomotor rhinitis

Picking at the Nose. Picking at the nose with the finger by a child was formerly considered to be a sign that the child had intestinal worms. It has been said that picking at the nose is common in those who have brain tumors However, picking at the nose is an expression of nervous tension and shyness Nervous or shy persons may have in due time either worms or brain tumors but picking at the nose is a sign of neither intestinal parasites nor brain tumors.

The Sense of Smell. The olfactory bulbs and their associated parts are in reality portions of the brain. The peripheral nerves arising from the bulbs are distributed to the mucous membrane of the upper portion of the nasal septum, the superior and middle turbinates, and the proximal part of the nasal septum. These distributions of the olfactory nerve can be identified by their yellowish brown color The free end of an olfactory cell is rodlike and reaches the surface of the epithelium, where it divides into small projecting olfactory hairs of microscopic dimensions The center for the sense of smell is said to be in the uncinate convolution.

To test the function of the olfactory nerve, nonirritating substances must be used, as pungent vapors affect mainly the trigeminal nerve. Suitable odorous agents are musk, oil of cloves and peppermint in convenient containers. It should be remembered that the perception of any single odor is lost in 3 or 4 minutes but is regained after 1 minute of rest. It is essential that the odorous material should enter the nostrils as a vapor or in a state of fine division; the act of smelling is usually assisted by sniffing, which is a modified inspiration. It is also necessary that the mucous membrane should be moist in order for the odorous particles to enter into solution on its surface.

The clinical symptoms relating to the sense of smell are *anosmia*, loss of the sense of smell, *hyperosmia*, increased sensitiveness of the sense of smell; and *parosmia*, subjective perversion of the olfactory sense.

Anosmia. The loss of the sense of smell, in the majority of instances, is due to local disease of the nasal mucous membrane, namely, chronic rhinitis, particularly the atrophic variety, and polyps or other new growths. The inhalation of irritating vapors or extremely foul odors may temporarily or permanently abolish the sense of smell. Paralysis of the trigeminal nerve will impair the olfactory power of the affected side. Loss of the power of smell may be a symptom, purely neurotic, of neurasthenia and hysteria.

Frequently the sense of smell is abolished because of injury or lesion of the olfactory bulb or tract. Falls or blows on the head, affecting the nerve in its course, may produce as the only symptom of injury a persistent anosmia. Caries of the bones supporting the tract or bulb, and basal meningitis or tumors involving the nerve, may be instrumental in causing olfactory anesthesia. Possibly from atrophy of the nerves, anosmia may be one of the symptoms of locomotor ataxia. Anosmia is sometimes congenital, resulting from imperfect development of the olfactory nerve tissue. Partial anosmia may be due to a lesion of the uncinate gyrus or to disease of one hemisphere.

Hyperosmia. Hyperosmia or abnormal sensitiveness of the sense of smell is, in its slighter degrees, not an uncommon symptom in neurotic individuals. More rarely the sensitiveness is extreme and is symptomatic of hysteria and neurasthenia.

Parosmia. Olfactory sensations without a physical basis, the apparent odors usually being unpleasant or offensive (*kakosmia*), are not infrequent as hallucinations in the psychoses. A bad odor may constitute the premonitory aura of epilepsy. Subjective kakosmia has been associated in a limited number of cases with tumor of the hippocampus.

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complaint is frequent hawking and clearing the throat, especially marked on arising in the morning and during or soon after meals The patient often interprets the symptoms as being due to sinusitis. Cough and hoarseness may be the chief complaint when laryngitis is present Often there are sensations of tightness, of dryness and fullness of the throat There may be difficulty in nasal breathing Some impairment of hearing may result from obstructions of the eustachian tubes Often in the morning, in attempts to clear the throat and the back of the nose of the tenacious secretion, vomiting may ensue. Generally speaking, a postnasal drip does not produce disease of the lungs or of the stomach, swallowing of the material is harmless and normal

Rhinitis. *Acute rhinitis* is characterized successively by a feeling of dryness in the nose, nasal obstruction, anosmia, and then a watery, irritating nasal discharge. Accompanying these manifestations often are sneezing, lacrimation, headache, fullness and discomfort in the ears, and fever.

Acute rhinitis *accompanies many and varied conditions. It is often the beginning* of an infection of the upper part of the respiratory passages.

Chronic Rhinitis. Chronic rhinitis *often follows an acute attack of rhinitis, or it* may result from a succession of mild attacks of coryza, or may be left after measles, scarlet fever or other specific infection. This condition is not contagious. It is frequently met with in those exposed to dusty occupations. The commonest symptom of chronic rhinitis is nasal obstruction, which seldom is complete It is generally intermittent, being worse after meals, in certain conditions of weather and at night During the day it may be negligible, but at night the nostrils become so obstructed that mouth breathing with all its discomforts is present On examination there is an engorgement of the vessels with chronic inflammatory changes in the mucosa

Hypertrophic Rhinitis. The complaint in hypertrophic rhinitis is of abundant, sometimes thick, mucopurulent discharge, occasionally stained with blood if much *force has been used in expelling it There is nasal obstruction, worse at night than* by day, and influenced by gravity so that the nasal chamber toward the pillow is most obstructed The obstruction may be sufficient to induce mouth breathing. The sense of smell is diminished, hence much of the perception often attributed to taste is lost The voice loses its nasal resonance. Discomfort or actual pain may be caused by pressure of a congested turbinal body on the septum.

Atrophic Rhinitis. Atrophic rhinitis is a chronic rhinitis of unknown origin and occasionally occurs in several members of a family The affection tends to disappear after middle life The condition is much less common in men than in women. It is characterized by atrophic changes in the nasal mucosa and *turbinated bones*, abnormal patency of the nasal fossa and a mucopurulent discharge with foul odor. The sufferer, however, is rarely aware of the odor, for as a rule the disease causes [illegible] the separa-

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Vasomotor Rhinitis (*Spasmodic Rhinorrhea*). Vasomotor rhinitis may be defined as an intermittent engorgement of the nasal mucous membrane associated with a free discharge of dilute mucus, frequently with paroxysmal *sneezing and suffusion* of the eyes. Often there are present a hypersensitivity of the nasal mucosa and some external irritation acting on the nasal mucosa. The psychoneurotic element is an important causative factor. Examination of the mucous membrane during an attack shows passive engorgement.

The attacks come with great suddenness, often in the early morning, and commence with a feeling of tickling or dryness in the nose. Perhaps the same sensation in the *conjunctivae* and a sudden attack of violent sneezing usher in a discharge of profuse watery mucus from the nostril. The sneezing may be so violent and uncon-

trollable as to cause ecchymosis of the conjunctivae. Often, as soon as the mucous membrane has been wetted by secretions, the attack ceases

Nasal Leprosy. Leprosy of the nose is manifested by chronic nasal obstruction, bloody nasal discharge and marked crusting. As time passes, there is destruction of parts of the nose with perforation of the nasal septum and maximal external nasal deformities.

The diagnosis is established by the presence of other symptoms of leprosy and by the demonstration of the bacilli in the nasal discharges Often the diagnosis of leprosy can be established by the administration of 10 drops of a saturated solution of potassium iodide in water to increase the nasal secretions. At the height of the secretion, about 2 hours after administration of the drug, the nasal septum and the nasopharynx are swabbed with a cotton applicator and the material is fixed on a glass slide by heat, stained with carbolfuchsin, and counterstained with methylene blue. *Mycobacterium leprae* is acid fast.

Screwworm Infestation (Cochliomyia americana) of the Nose. The common site of screwworm infestation in man is the nose, but infestation of nasal sinuses, pharynx, throat, mouth, ear, orbit, eyeball and open wounds may also take place. The chief predisposing factor in rhinal myiasis is a pre-existing pathologic condition of the nose. A cut, scratch or abrasion of the skin is necessary to attract the female screwworm fly. Sleeping in the open invites infestation The eggs hatch out 24 hours after being deposited in a favorable environment The symptoms include partial obstruction to breathing on the affected side and a feeling of discomfort accompanied with a strange sensation at the root of the nose that becomes an intense pain. Sneezing may occur at the onset, and severe headache may persist. A serosanguineous nasal discharge of offensive odor accompanies these symptoms. With the onset of this discharge, the patient may clear his throat repeatedly, expectorate frequently and cough up a purulent material that may contain living or dead larvae. Removal of the larvae is accomplished mechanically and by the use of drugs Chloroform applied locally and as a vapor is the drug of choice Although screwworm infestation occurs chiefly in the Southern states, cases have been observed as far north as Missouri and Illinois

Diseases of the Nasal Septum. The septum in most noses is somewhat irregular and rarely is placed evenly between the nares.

Ulcers. A commonly occurring ulcer of the nasal septum develops as the result of habitual picking of the nose with the index finger, a habit caused by nervous tension. The inception is manifested as a septal erosion from repeated trauma The urge to do more picking of the nose is made stronger by the irritation and discomfort The septum may be deeply injured and the mucosa may be denuded

Rare causes for ulcers of the nasal septum are syphilis and trauma from irritating chemicals and particulate matter such as organic and inorganic particles or dusts

Once the ulcer is established, there ensue nasal irritation and epistaxis If syphilis is the cause, there is a foul nasal discharge with destruction of the septum

The ulcer is identified by endoscopic examination

Deformities. The deformities are classified as spurs, deviations, and combinations of spurs and deviations. If of a sufficient degree, these deformities originate the complaint of nasal obstruction and inability to clear one or both nostrils Any of the sequelae of mouth breathing, however, may be due to aberrations of the nasal septum.

A spur is found to consist of a crust, a spina or a thickening It is chiefly cartilage, but it is often present at the junction of cartilage and bone, both of which enter into its formation. Deviations of the nasal septum are almost always more pronounced in the cartilaginous portion of the septum than in the bony portion.

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Atrophic rhinitis symptomatically may resemble the symptoms of foreign bodies, rhinolith, empyema, lupus or suppurating adenoids

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of the nose is determined by roentgenologic examination. The diagnosis of malignant disease is established by biopsy.

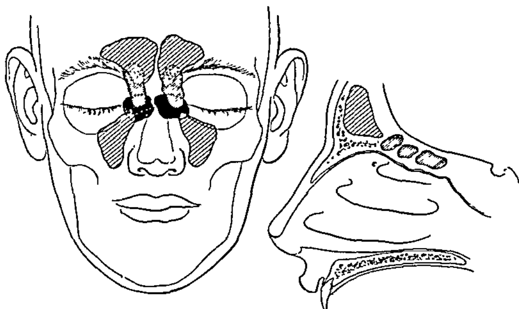


Fig 4-2 Accessory nasal sinuses

The Accessory Sinuses. The accessory sinuses or air cells of the nose are the frontal, ethmoidal, sphenoidal and maxillary (Fig. 4-2). They vary in size and form in different individuals These sinuses are lined with ciliated mucous membrane which is directly continuous with that of the nasal cavities

The *frontal* sinuses are frequently the seat of suppurative inflammation, which gives rise to pain and tenderness in the supra-orbital region and to a discharge from the corresponding nostril This discharge can be seen coming from beneath the anterior extremity of the middle turbinated bone Owing to the proximity of the opening into the maxillary sinus, pus coming down the hiatus from the frontal sinus may pass into the maxillary sinus, thus simulating disease or producing disease of that cavity too

The *ethmoidal* sinuses or cells, anterior, middle and posterior, three on each side, lie between the sphenoidal sinus posteriorly and the lower extremity of the frontal sinus anteriorly The region of the ethmoidal cells is that from which mucous polyps of the nose take their origin. These polyps are a common accompaniment of suppuration of the accessory nasal cavities Caries affecting the anterior cell of each sinus may extend into the orbit, and the pus may form a fluctuating tumor above the inner canthus of the eye It is to be recalled that a meningocele may be present in this same location

The *sphenoidal* sinuses are the most posterior, lying still farther back than the ethmoidal sinuses They open into the spheno-ethmoidal recess above and posterior to the superior turbinated bone Discharge from them goes into the pharynx and can be seen with the rhinoscopic mirror.

The *maxillary* sinuses lie, one on each side of the nose, beneath the orbit and to the outer side of the nasal fossa The sinus opens into the nose by a slit-like opening into the middle meatus about its center, posterior to the hiatus semilunaris and 1 inch (2.5 cm) above the floor of the nose When the opening is close to the hiatus, liquids may run into it from the hiatus

The inflammatory and infectious diseases of the maxillary sinus originate by extension from either the nose or the teeth The sinus is the seat of tumors, often malignant, and of inflammation, the latter accompanied by an accumulation of mucus or pus The walls of the sinus are thin, so that a tumor, bulging forward, causes a protrusion of the cheek. The tumor presses inward and obstructs the breathing through the side of the nose, or it pushes upward and causes protrusion of the eye by encroaching on the orbit

Perforation. Perforating ulcerations of the bony part of the nasal septum are often due to syphilis, but when the cartilaginous septum only is attacked, the ulceration is probably not due to a specific process. An ulcer of the nasal septum may form and perforation may take place without the patient knowing of its occurrence The symptoms complained of are a sense of dryness, irritation in the nose, the separation of crusts and, occasionally, free epistaxis. When perforation first occurs, there is often a whistling sound caused by the passage of air through the small opening This gives much annoyance to some patients but they can be reassured, since the sound generally ceases when the opening increases to a larger permanent position

Nasal Obstruction. One of the most frequent and most important consequences of nasal disease is obstruction to respiration The harmfulness of mouth breathing entailed in cases of severe disease is definite

Since nasal obstruction is a factor in numerous nasal affections, and since many of its possible consequences are not always recognized, an enumeration of the causes and symptoms is worth while Inactive alae nasi, which permit of diminished ventilation of the nose and arrested development of the nasal passages, lead to deviation of the nasal septum and often to defective development and growth of the upper maxillae with arching of the palate, V-shaped alveolar arch and crowded teeth There is a tendency to frequent and prolonged nasal catarrh and later to hypertrophic rhinitis Postnasal catarrh and increase in adenoid tissue often follow.

Catarrh of the eustachian tubes in either acute or chronic otitis media may develop as a part of the general pathologic processes that follow nasal obstruction

The symptoms of nasal obstruction are difficulty in clearing the nose of mucus, noisy nasal respiration with sniffling, heavy breathing and snoring, loss of nasal resonance, alterations of the voice, anosmia or loss of the sense of smell, and deformity of the thoracic wall Well-developed mouth breathing is associated with a typical facies, dry mouth, spongy gums, imperfect mastication of the food and slowness in eating or necessity of bolting the food

Nerves of the Nose. In addition to the olfactory nerve the nose is supplied by the nasal, infratrochlear, and infra-orbital branches of the fifth nerve, hence the eyes water when the nose is injured In certain cases of neuralgia affecting the ophthalmic division of the fifth nerve, pain is felt along the side of the nose Because the nasal nerve enters the skull from the orbit through the anterior ethmoidal foramen, it may be involved in disease of the ethmoidal sinuses.

Nasal Polyp. Polyps are the commonest tumors of the nose. They are benign tumors which usually do not become malignant, however, they tend to recur after removal

The causes of nasal polyps are unknown These tumors are often associated with hyperplastic rhinitis

Mucous polyps arise from the outer wall and principally from the margin of the middle meatus and the cells of the ethmoidal labyrinth The symptoms of nasal polyp develop slowly and the patient sometimes becomes so gradually accustomed to the condition that the disease is often well marked when the patient is first examined. The symptoms are those of nasal obstruction and its consequences.

Nasopharyngeal Polyp. Nasopharyngeal polyps are usually unilateral and solitary A single polyp in the nasopharynx may have its origin in the antrum and by growth pass into the nose through an accessory ostium maxillare. The symptoms are those caused by one-sided nasal obstruction and catarrh. There is increasing discomfort as the polyp descends into the pharynx

Malignant Tumors. Malignant tumors of the nose are rare. The symptoms of a malignant nasal tumor may commence by the presence of nasal obstruction and discharge, and bleeding spontaneously or on slight manipulation. Spontaneous bleeding occurring in a middle-aged patient arouses suspicion of the presence of malignant disease. The extent to which a malignant tumor has involved the nose or the bones

Inflammation and obstruction may extend to the lacrimal passages, the conjunctival and finally the orbital tissues, producing orbital cellulitis and periostitis. Extension of infections from an accessory sinus may cause a great swelling and ptosis of the eyelids, chronic conjunctivitis, blepharitis, photophobia, dilatation of the pupil and blepharospasm. In such ocular involvements exophthalmos and some impairment of the mobility of the eyes are common. These conditions are serious illnesses and always are accompanied by marked constitutional symptoms, which are manifested by high fever and violent pain in this region.

The aural symptoms arising from a chronic suppuration of the sinuses are tinnitus, vertigo and earache. Noises in the ear as a result of eustachian catarrh may be the first discomfort to attract the patient's attention

Headache, face-ache, hemicrania and neuralgia, though commonly of origins other than the sinuses, often require an exploration of the sinuses Pain in the face arising from sinus disease may present a morning periodicity, increasing for some hours after the patient arises in the morning and often disappearing as the day goes on This periodicity has been explained as the result of accumulation and retention of secretion during the night The secretion then escapes from the cavity during the first hours of physical activity

The diagnosis of chronic sinusitis is made on the basis of the symptoms and of examination for signs of rhinitis, particularly in the region of the ostium of the sinus, together with evidences of discharge in the nose and nasopharynx. The presence of polyps at once points to chronic ethmoiditis In many cases roentgenologic examination will reveal changes in the bone or thickening of the linings of the cavities of the sinuses Roentgenograms of the sinuses often reveal the presence also of hyperplastic thickening of the membranes and of formation of polyps in the sinuses. Finally an exploratory puncture and washing of the sinuses to reveal pus if present may be required for diagnosis.

There are but few physicians left who regard a chronic sinusitis as of much importance as a focus of infection The prognosis is usually for spontaneous recovery or, at least, for temporary alleviation of symptoms

Voice Dynamics and the Ethmosphenoid Epiglottidean Syndrome. The nose and the nasal cavities act as resonating chambers for the voice whereby sounds produced in the larynx are amplified and changed in timbre. A lack of nasal resonance, as observed in nasal obstruction, is termed rhinolalia clausa

The patients complain, usually in the morning, that they are not in good voice. The alteration in voice and the hoarseness clear up during the day. Vocalization and swallowing usually dispose of the effete mass that has accumulated during the night The patient finds it difficult to start phonation, and his throat tires quickly

In some patients the symptoms may be referable to involvement of the muscles of the pharynx and their nerve supply To a singer this may be a devastating malady. Pressure in the laryngeal structure from even a small amount of pus may be sufficient to interfere with the normal emission of the pus by coughing As the disorder advances pus accumulates in large quantities and remains in evidence when the epiglottis is examined

In some patients there may be a partial or total loss of taste or smell, a ticklish and tight feeling about the throat and blocking of the ears, with or without spasmodic cough Less frequently patients hear tingling noises, an echo or a vibration Pus may be found in the nasopharynx, and redness of the tympanic membrane without an impairment of hearing.

Cysts and Benign Tumors of the Sinuses. The maxillary sinuses may contain mucous retention, serous, periodontal or dentigerous cysts. Mucous retention cysts are the common cysts often reported by the roentgenologists. A cyst of the periodontal type arises from the root of a pulpless tooth The bone is eroded from the

Diseases of the Accessory Sinuses. Suppuration may arise primarily from direct infection of an accessory sinus or secondarily from some intranasal disease. Among the acute infectious diseases which give rise to sinusitis are influenza, pneumonia, measles, scarlatina, smallpox, cerebrospinal meningitis, diphtheria, erysipelas and, more rarely, mumps and gonorrhea Coryza and all processes of nasal disease associated with pus formation may induce empyema in the accessory cavities. The anterior group of sinuses is much more frequently affected than are the posterior groups. Of the anterior cells the maxillary sinuses are the ones most often involved, the ethmoidal next, and the frontal sinuses least often

Acute Sinusitis This forms a part of many acute catarrhs which invade the sinuses by direct extension from nasal coryza Acute exacerbations are not uncommon in the course of chronic empyema Bathing in a public swimming pool, particularly if diving is done, may lead to infection of the nose and sinuses Acute sinusitis is generally met with in adult life but is not unknown in childhood.

The symptoms of an acute sinusitis frequently form a part of acute nasal coryza. However, if during an acute nasal coryza there occurs pain in the region of a sinus accompanied by tenderness on pressure over the cavity, sinusitis is suspected. Lacrimation, photophobia, edema or a light congestion of the eyelid with proptosis, and deep-seated headache also suggest the implication of a sinus More than one cavity may be affected at the same time The occurrence of a chill or of a rise in temperature would indicate more than a simple catarrh in a patient suffering from acute rhinitis Relief of pain follows a discharge of mucus, which may be bright yellow and blood-stained or mucopurulent, or relief follows a free gush of pus which sometimes is very offensive both to smell and to taste

On examination there is usually evidence of acute rhinitis, or the middle turbinal will be congested, infiltrated and pushed against the septum, and the meatus below it will be clogged with stringy mucus and, later on, with mucopurulent material Transillumination may direct attention to the maxillary sinus, and puffiness of the forehead or fullness or duskiness of the eyelid on one side will point to the frontal or the ethmoidal cavities When the posterior group is affected, the rhinoscopic mirror will show a deeply congested appearance of the pharynx and anterior sphenoidal wall, and mucopus will ultimately be visible above the superior turbinal on the posterior pharyngeal wall Most patients who have acute sinusitis recover spontaneously Complications very rarely result, but sometimes occur during the course of a chronic sinusitis as the result of an acute exacerbation

Chronic Sinusitis Chronic sinusitis in the accessory sinuses is common In many cases roentgenologic examination reveals clouded mucous membrane of the sinuses, but this does not necessarily imply active disease

The maxillary sinuses are those most often affected Patients afflicted with empyema or chronic sinusitis frequently seek relief on account of discharge or of obstruction or of a chronic cold in the head

The symptoms of chronic sinusitis may be grouped as (1) nasal symptoms, (2) nasopharyngeal symptoms, (3) ocular symptoms, (4) aural symptoms and (5) headaches

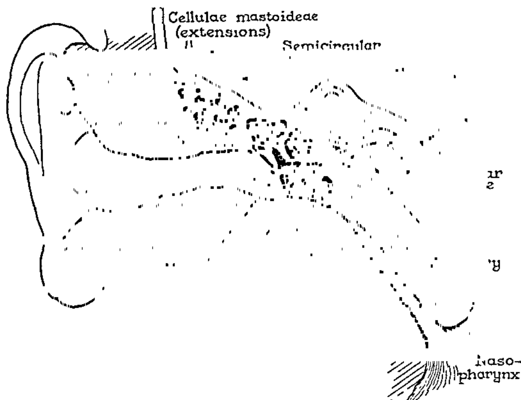
The nasal symptoms are nasal obstruction and nasal discharges The obstruction may be unilateral or bilateral. It is usually more marked in the morning hours than at other periods and is more intense with the increase of nasal inflammation The discharges may flow posteriorly and the obstruction may be slight and the secretion scant in amount so that the patient for years has swallowed it unconsciously Disorders of the senses of smell and taste are often indicative of the disease There may be parosmia or anosmia, or there may be kakosmia. The presence of kakosmia is suggestive of sinus suppuration. The patient is seldom aware of the odor.

The symptoms in the nasopharynx and the larynx are those of a postnasal irritation or low-grade inflammation.

and frostbite is therefore common. Injuries and wounds of the cartilage occur readily and are slow to heal.

Discoloration. A livid or *bluish* tint of the external ear is usually indicative of general cyanosis A frostbitten ear is at first white, but when it becomes thawed the skin is cyanotic. A *blue-black* discoloration of the cartilages of the ear occurs in ochronosis (usually with alkaptonuria). A swollen, discolored pinna may be due to *injury* or *hematoma.*

Angioma, or enlargement of the blood vessels, not infrequently affects the external ear and not only may disfigure but also may show a tendency to extension to the scalp, face and neck In some instances these angiomas are jet black and fissured, and contain hair



Redrawn from Max Brödel, unpublished drawings, by permission of W B Saunders Company

Fig 4-3 The ear

The External Meatus. The external auditory meatus extends from the concha to the drum head (Fig 4-3) In order to look into the ear and see the membrane, it is necessary to straighten the canal by pulling the auricle outward, upward and backward The general direction of the canal in the adult person is from without, downward, inward and slightly forward In a child upward traction is not so necessary as in the adult In childhood the length of the canal is approximately the same as in adult life, but the bony part is still in a cartilaginous condition.

The external opening of the meatus is oval, but farther in, the canal is more nearly circular In examining the meatus, the otoscopic attachment of an ophthalmoscope or a speculum and head mirror are used.

Below and in front of the ear is the temporomaxillary joint, and just posterior is the glenoid lobe of the parotid gland. When the gland is inflamed and swollen, it presses on the cartilaginous canal and produces pain; and in case of suppuration,

tooth to the sinus by means of granulation tissue formation. Dentigerous cysts are of congenital origin and are mentioned in association with tumors of dental origin

These cysts do not produce symptoms unless they have attained space-occupying proportions sufficient to give pressure symptoms The symptoms consist of pain. There may be swelling of the cheek and bulging of the lateral part of the adjacent nasal cavity Diagnosis is established by roentgenographic examinations and needle puncture Small cysts require no treatment.

Papillomas, adenomas, lipomas, hemangiomas, osteomas, chondromas, gliomas and mixed tumors occur mainly in the frontal and ethmoidal sinuses. These tumors usually do not give symptoms until they have occupied all the available space in the sinus. After this they produce symptoms from pressure and by eroding adjacent bone and interfering with the function of other organs, such as causing a unilateral exophthalmos by extending into the orbit

Malignant Tumors of the Sinuses. Malignant tumors which affect either the paranasal sinuses or the nasal cavities as a rule arise in the sinuses. These tumors, consisting equally of carcinomas and sarcomas, arise most frequently in the maxillary sinuses. However, they do arise in the ethmoidal and the frontal sinuses

When the tumor extends from the sinus, it erodes bone There is pain, and often there are severe epistaxis and nasal obstruction A purulent bloody nasal discharge is common. Malignant tumors in the antrum cause pain in the teeth and cheeks, sensory disturbances of the skin, and swelling of the cheek. There is often bulging into the nose and hard palate, or unilateral exophthalmos The lymph nodes on the ipsilateral side are enlarged, and metastasis ensues to distant regions.

The diagnosis is made on the basis of roentgenographic studies which reveal a mass or defect in the bones of the affected sinus Biopsy of tissue from the sinus or from the nose is conclusive

Malignant Tumors of the Nasopharynx. Malignant tumors of the nasopharynx are usually highly anaplastic carcinomas, usually designated by such terms as lympho-epithelioma or transitional-cell carcinoma They metastasize early, and it is usually the metastatic lesions that first attract attention—swelling in the neck, or pain or deafness in one ear Headache, sore throat, epistaxis and nasal obstruction are frequent complaints Cranial nerves may become involved, with resultant diplopia or optic atrophy Signs due to involvement of the fifth, seventh and other cranial nerves are occasionally demonstrable The local lesion in nasopharyngeal lympho-epithelioma may escape detection by expert otolaryngologists for as long as 6 months after the tumor has been histologically identified in a metastatic cervical node

THE EAR

The external ear (auricle, pinna) is composed mainly of a cartilaginous framework covered with thin skin The lobe, which is the lower part of the ear, is composed of dense connective tissue containing fat The large concavity leading into the meatus is the concha

The external auditory meatus, the tympanum and the eustachian tube are formed from the first branchial cleft in the fetus A failure of any portion of the cleft to close normally may leave small sinuses or depressions in the neighborhood of the ear and these may persist after birth as congenital fistulas More severe deformities may result from cleft abnormalities resulting in absences of parts or all of the ear

Ears that are unusually prominent, long or misplaced, with absence of helix, anthelix or lobule, are marks of imperfect physical development. These abnormalities do not necessarily carry stigmas of degeneration An unusual protrusion of large auricles from the sides of the head is the commonest of all ear deformities.

The loss of the auricle does not cause much, if any, decrease in sound perception. The subcutaneous tissue of the ear is well supplied with blood Owing to the absence of fat, the exposed condition of the blood vessels renders the ear sensitive to cold,

Neuralgia, or recurring pain in one ear similar to the episodes of pain from tic douloureux, is experienced. Arthritis of the temporomaxillary articulation is accompanied by earache. Angina pectoris and, if in the right ear, aneurysm of the innominate artery, may give earache. Affections of the tongue may be accompanied by otalgia. Herpes zoster oticus may be preceded or followed by severe pain in the ear.

Discharges From the Ear. A fracture of the base of the skull may cause an aural hemorrhage, followed by the escape of *clear cerebrospinal fluid.*

Rupture of the tympanic membrane, either as a result of injury or consequent on otitis media, may be responsible for a discharge of *blood.*

A flow of *pus,* otorrhea, may be either acute or chronic and while it may be due to a polyp or abscess of the external meatus, it is, in the majority of cases, an evidence of otitis media with or without complication.

Diseases of the Membrana Tympani. Reflected light from a head mirror or an otoscope directed through the meatus by a speculum reveals the membrana tympani Extending downward from its center is a small cone of light Any depression or bulging of the membrane will cause this cone of light to be altered in its position or not be present at all. From the center of the membrane upward extends a line which indicates the point of attachment of the long handle of the malleus Stretching across the upper portion is the membrana flaccida.

During the course of acute rhinitis, pharyngitis or influenza, blebs or bullae filled with blood serum or blood may develop in the skin of the deep portion of the external canal and on the drum. These may be present before there are symptoms of otitis media. The blebs appear as purple blisters which break at touch and yield bloody serum, leaving the skin or the drum wet and red Soon the blebs break and cause a thin bloody discharge. Often synchronously with the sanguineous discharge from the ear there is relief of the pain

Rupture. The ear drum may be ruptured by the introduction into the canal of pins or sticks for scratching or removal of wax, flat-handed slaps or boxes on the ear; the compression of explosion, as by artillery fire, too rapid decompression, as occurs in divers and in occupants of aircraft after rapid descent from high altitudes

The symptoms of ruptured drum are sudden and intense pain in the ear followed by deafness, loud tinnitus and perhaps vertigo, nausea and vomiting If infection follows and acute otitis develops, otoscopic examination reveals fresh or dry blood in the canal and on the drum The perforation may be visible Bloody crusts in and about the ruptured membrane will be present for several days. Increasing pain, fever and a seropurulent discharge denote the presence of otitis media

Diseases of the Middle Ear. Otitis Media *(Infections of the Middle Ear).* Infections of the middle ear pass up the eustachian tube from the pharynx and the nasal cavities. The infection may pass thence to the mastoid antrum and mastoid cells On pus formation and suppuration of the middle ear the pus usually obtains an exit by perforating the tympanic membrane and discharging through the external auditory meatus

In instances of retropharyngeal abscess or suppuration of the middle ear pus may pass down the eustachian tube and escape through the nose

In a retropharyngeal abscess originating in a vertebra the pus may pass through the fascia or behind it, extend laterally and appear under the sternocleidomastoid muscle While behind the fascia, the pus may be in contact with the base of the skull, and if so the infection may pass through the porous bone and involve the meninges and the brain In rare instances the pus may perforate the bone below and anteriorly and involve the jugular vein and the internal carotid artery.

In suppurations of the middle ear, if the posterior bony wall of the auricular canal is perforated, the infection may involve the facial nerve with facial paralysis ensuing The brain also may be reached by the infection extending through the internal ear through the fenestra ovalis and rotunda, and the internal meatus, and

pus may discharge through the external meatus, gaining access to the canal through fissures in the cartilage. The cartilaginous portion of the meatus contains sweat glands, sebaceous glands and hair follicles. There are only a few glands in the upper posterior portion of the bony meatus.

Impaction of Cerumen. Cerumen is the normal secretion of special ceruminous glands in the cartilaginous portion of the external auditory canal. Excessive accumulations of cerumen may give symptoms When symptoms are present, the mass has formed, and it may then move with motion of the head or may swell on the entrance of sweat or water and produce complete obstruction A complete obstruction causes deafness, tinnitus and a full, stopped-up feeling in the ear. At times there is a cough from a vagus nerve stimulation There may be pain or vertigo if the mass presses against the drum If the auditory canal has been filled with the wax, there may be dilatation of the canal, or erosion of the skin and granulation tissue may result. Bleeding ensues on removal of the wax, healing follows readily.

Furuncle. A furuncle of the external auditory canal is due either to the entrance of pyogenic organisms into the subcutaneous tissue by way of hair roots or follicles or to an infection of sweat glands

The commonest predisposing cause of furuncle of the auditory canal is an acute or a chronic dermatitis of the canal The process begins with pain of increasing intensity in the ear with throbbing, there is pain on movement of the lower jaw, and wide opening of the mouth may be impossible because of the pain Local pressure on the pinna, or auricle, or motion of this part is painful There may be a general aching and at times a fever

The diagnosis of furuncle of the auditory canal is made easily on inspection of the canal, especially if the ear drum is not congested or is not perforated. A roentgenologic examination should be made if there is doubt about involvement of the mastoid cells

External Otitis. Some forms of external otitis may be due to otomycosis An otomycosis is usually an accompaniment of a mycotic infection of the skin. The ear feels sore and tender, chewing may be painful The auditory canal often contains soft semifluid wax and debris of flecks of a white foamy substance. As the disease progresses, the ear is tender, and chewing is painful. The canal is sometimes completely filled with soft, moist, sebaceous-like detritus, which often has a greenish color due to a secondary infection After the ear has been cleansed, the canal wall is found to be red, with excoriation of the epithelial lining The drum is not affected In the severely affected ear the canal is swollen, often obliterated and very painful. The pain is worse at night than by day and there may be fever An otomycosis is diagnosed by identifying the fungus in the discharges from the affected ears.

The external auditory canal is affected in many forms of dermatosis

Pain in the Ear. Earache. USUAL CAUSES. The most frequent cause of severe pain in the ear (earache) is otitis media secondary to many illnesses such as scarlet fever, epidemic influenza, acute simple rhinopharyngitis or tonsillitis, measles or diphtheria. It is commonest in children and may explain an obscure infantile illness with fever

OTHER CAUSES. Pain referred to the ear or about the mastoid process when there is no local cause for such symptoms is a reflex or referred otalgia Common causes of these secondary otalgias are exposed dentine and inflamed pulp or dying nerves of the teeth on the same side, particularly in the mandibula; unerupted, impacted or infected molar and wisdom teeth which may cause severe, deep, boring earache of long duration. Acute inflammation or ulcerative processes exposing nerve ends in the nasopharynx, pharynx, laryngopharynx and larynx may give rise to otalgia Malignant growths, even small ones, of the nasopharynx are prone to cause this symptom. A sphenopalatine ganglion neuralgia often causes pain in the ear or in the region of the emissary vein on the posterior surface of the mastoid process.

persistent mucopurulent discharge constantly or intermittently. In such a condition healing may eventually take place but there is permanent impairment of hearing Owing to impairment of function of an injured labyrinth, an impairment of hearing may become manifest after all signs of infection have ceased

The serious complications of acute otitis media are suppurative mastoiditis, serous or purulent labyrinthitis, meningitis, extradural brain abscess and lateral sinus thrombosis.

Suppurative Mastoiditis. Suppurative mastoiditis is a complication of otitis media or it occasionally occurs after fractures of the skull. Once the infection is established in the mastoid cells, it tends to persist and to suppurate

The common etiologic agent is the hemolytic streptococcus However, any one of the pyogenic organisms may be present such as the staphylococcus or the pneumococcus.

There is a rapid vascular engorgement with edema and infiltration and the production of a mucopurulent exudate The mucosal cells degenerate, so that the bone is deprived of blood supply, and the cell walls disintegrate. Large cavities are present in the well-pneumatized mastoid form and if the cortex is thin or thinned, perforation ensues If the aditus and antrum are large enough to furnish adequate drainage into the middle ear, resolution can take place.

The symptoms depend on the severity of the suppurative process Pain is present in the ear and over the mastoid area. Fever (temperature up to 103 F or more) which is present for several days may then subside except for afternoon rises The recurrence and the continuation of the fever indicate a more severe process. There are nausea, vomiting, anorexia, constipation and increasing weakness.

Tenderness, which may be widespread, is present over the mastoid antrum There is often edema of the skin and soft parts, and swelling of the posterosuperior wall of the external auditory canal. The tympanic membrane is bulging and perforated. There is often deafness of the conduction type without tinnitus.

A polymorphonuclear leukocytosis is the rule. The urine may contain albumin, depending on the amount of fever The roentgenogram reveals the degree of bone changes as well as the degree of pneumatization of the cells. The latter is helpful in determining prognosis, for the highly pneumatized cells are more easily and widely destroyed.

Labyrinthitis. The labyrinth is often affected from the toxic agents of infections without the entrance of bacteria. Bacteria may enter the labyrinth as the result of trauma, surgical or otherwise, or from middle ear disease In widespread labyrinthitis there may be destruction of essential structures and loss of function

The invasion of the cochlear portion of the labyrinth causes tinnitus and deafness Invasion of the vestibular apparatus produces varying degrees of vertigo, nystagmus, temporal or retro-ocular headache, vomiting and mild weakness of the facial muscles In diffuse involvement of the labyrinth the patient becomes very ill with severe vertigo which makes it impossible to stand alone. The patient lies absolutely still The room seems to turn toward the diseased ear. The slightest movement brings on violent vomiting

The diagnosis of labyrinthitis depends on the accurate testing and evaluation of the turning, caloric and fistula tests by one trained in employing these tests and interpreting the findings Acutely ill patients are not subjected to these tests

Tuberculosis. Tuberculosis of the middle ear is rare except in young adults during the advanced stages of pulmonary tuberculosis. The infection seems to be brought to the ear as a blood-borne infection or when there are serious deep lesions of the pharynx or nasopharynx In the latter instances the infection reaches the ear through the eustachian tube.

Once in the ear, a tuberculous infection causes widespread destruction of the tympanic membrane, auditory tube, mastoid cells, and bone of the labyrinth. In-

then to the brain. The infection may extend to the attic and the antrum and perforate the roof of these structures and form a subdural abscess in the middle cerebral fossa. Extension of an inflammation from the antrum and mastoid cells may enter the posterior cerebral fossa to involve the lateral sinus, causing a lateral sinus thrombosis, or produce a cerebellar abscess

ACUTE OTITIS MEDIA. In an acute otitis media the fluid content of the middle ear is either serous or purulent Mild infections of the middle ear occur which do not perforate the tympanic membrane. When the fluid of the middle ear is serous, the otitis may be of allergic origin. However, all forms of otitis media are to be considered infectious in origin until proved different. The bacteria most commonly involved are the hemolytic streptococci, the *Hemophilus influenzae* and all forms of pneumococci, staphylococci, and, in rare instances, such organisms as the *Klebsiella pneumoniae*. In most cases these organisms enter the auditory canal through ethmoid cells or through the eustachian tube by continuity of tissue, aided by such mechanical devices as blowing of the nose, sneezing and coughing In instances in which the drum has been perforated previously, the organisms may enter from the external auditory canal. *However, in most instances of acute inflammations of the middle* ear the organisms enter from the nasal cavities, the paranasal sinuses, the nasopharynx and the pharynx

In the beginning of otitis media the pain may be mild, but as the inflammatory process spreads, the pain becomes more severe The pain is often the boring, lancinating type that spreads into the occiput, temples and teeth and is made worse by *coughing, sneezing or swallowing Except in very mild infections there is fever.* The height of the fever indicates to some extent the severity of the infection· In mild cases the temperature will reach 101 or 102 F (38 3 or 38.9 C); in severe infection it may be as high as 104 F (40 C) The fever usually continues 4 or 5 days with morning remissions and ceases by lysis Synchronous with the onset of the fever there are malaise, anorexia, vomiting, pain in the back and limbs and constipation The *pain, and often the fever, disappears on perforation of the drum*

The drum is usually retracted It may appear injected or may have a grayish color or a yellow cast and often is shiny. At times bubbles of fluid or a fluid meniscus may be visible through the tympanic membrane.

CHRONIC SUPPURATIVE OTITIS MEDIA Chronic suppurative otitis media is manifested by an intermittent, purulent discharge from the ear, which accompanies respiratory infections During acute exacerbations the discharge from the ear increases During an exacerbation, if the discharge stops, often there are pain and fever.

The diagnosis is established by otoscopic examination. The perforation of the drum is identified A central perforation without involvement of the annulus tympanicus differentiates this form of otitis media from the more severe forms

The perforation of the tympanic membrane in the severe necrotic types of otitis involves the peripheral parts of the drum. The opening is irregular in shape and may represent destruction of from one half to two thirds of the drum There may be granulation tissue or a polyp inside the perforation

Masses of debris appearing on the attic and the tympanic atrium which arise from squamous epithelium growing through the perforation in the drum are known as *cholesteatoma*. The term is derived from the content of fat and cholesterol of the masses of debris.

The perforation may be a large defect in the tympanic membrane through which the promontory of the ossicles may be visible. Deafness of the conduction type is variable in its severity Roentgenologic examination may reveal a nonpneumatized type of mastoid process.

COMPLICATIONS OF OTITIS MEDIA The complications of otitis media depend on the severity of the disease. The *infectious* process may become subacute with a

vertigo of central nervous system origin develops slowly over a long period. There may be associated nystagmus and falling. The diagnosis of these lesions, however, lies within the field of neurology and neurotology.

Types of Dizziness and Vertigo. DeWeese emphasized that it is not wise to focus all of the attention on hearing and labyrinthine function, for in the great majority of patients complaining of dizziness the results of functional examination of the ear will be normal.

Cerebral anoxemia may produce dizziness. Arteriosclerosis and hypertensive cardiovascular disease often produce a constant feeling of uncertainty or intermittent mild attacks of dizziness. In postural hypotension dizziness occurs when the patient rises suddenly from a recumbent or sitting position to the standing position. Pernicious anemia or any severe anemia may produce transient or recurrent dizziness as a result of cerebral anoxemia

Sudden and more prolonged cerebral anoxemias are produced by paroxysmal auricular fibrillation; aortic stenosis with insufficiency, arteriosclerotic heart disease (Adams-Stokes disease), and carotid sinus hypersensitivity. In some cases of dizziness from these causes it may be necessary to withhold a final opinion until the patient can be observed during an attack.

Dizziness is not a feature of brain tumor or other destructive disease inside the calvarium unless there is depression of function of the inner ear on one or both sides. Dizziness is a feature of lesions of the cerebellopontine angle and of the brain stem In cerebellopontine angle lesions there is loss of hearing, tinnitus, corneal anesthesia, fifth and seventh cranial nerve involvement, ataxia, and intracranial hypertension.

Chronic and recurring dizziness cannot be attributed to head injuries unless there is a persistent loss of hearing in a patient who had normal hearing prior to the accident. However, concussion can give rise to dizziness, tinnitus, headache and other symptoms without any positive physical findings perhaps as the result of multiple small hemorrhages. Compensation neurosis and outright malingering are common and may cause diagnostic difficulties in those who have had head injuries.

In labyrinthine hydrops there are paroxysmal attacks of whirling vertigo, usually with abrupt onset, almost always accompanied with nausea and vomiting These attacks last an hour or two and subside There is complete freedom from vertigo between attacks There is an accompanying perceptive hearing loss, frequently fluctuating, almost always progressive and usually more severe in one ear than in the other. Tinnitus, most commonly persistent between attacks and frequently fluctuating, is present The associated hearing loss is often a flat, low-tone perceptive loss, and the caloric reaction is hypoactive

Acute toxic labyrinthitis often follows an acute febrile disease, indiscretion in consumption of food or alcohol, or the use of any type of drug. In this syndrome there is a gradually increasing whirling vertigo lasting 1 to 3 days, followed by a slow subsidence of symptoms within a period of a week. There is no associated hearing loss or tinnitus

When the end-organ is suddenly and completely destroyed, either by injury or by hemorrhage, there are a sudden, overwhelming vertigo, nausea, vomiting, loud tinnitus and complete loss of hearing A slow compensation takes place over a period of 10 to 20 days, and gradually the opposite labyrinth controls reasonably well the function previously presided over by both labyrinths.

The commonest cause of dizziness is a functional disorder. The diagnosis should be made on the basis of positive evidences of the existing neurosis This is one of the most important diagnoses to be made, lest there be created an iatrogenic disorder.

Ménière's Disease. Ménière's disease is characterized by sudden attacks of vertigo, with tinnitus or incomplete deafness in one or both ears.

Ménière's disease may be attributable to disease of the labyrinth either hemor-

vasion of the facial canal and paralysis of the facial nerve ensue. A destructive form of labyrinthitis with deafness may occur. These widespread destructions may take place with a minimum of symptoms.

Examination discloses that the drum is perforated and discharges a foul purulent material. There is a perception type of deafness. The diagnosis is established by the demonstration of tubercle bacilli on culture and by guinea pig inoculation of the suspected material

Syphilis. Congenital syphilis frequently engenders deafness by destruction of the cochlea and semicircular canal apparatus Infants thus affected are born with total deafness. In some instances of congenital syphilis, osteomyelitis of the labyrinth or syphilitic neuritis of the cochlear nerve does not occur until between the fifth and fifteenth years of life.

The diagnosis is based on the history and the presence of Hutchinson's triad: (1) interstitial keratitis, (2) Hutchinson's teeth and (3) deafness Often perforation of the bony part of the nasal septum is present.

In acute acquired tertiary syphilis which is present in the nasopharynx the process will extend to the membrana tympani Generally such an extension is made by pyogenic organisms rather than by the *Treponema pallidum*. Once in the ear, the syphilitic process is very destructive The labyrinth is destroyed and sequestra are formed There is a profuse purulent discharge from the middle ear There are severe labyrinthine symptoms which soon subside as total deafness ensues. The diagnosis is established from the history, the examination, and the strongly positive serologic reactions

Tinnitus. Subjective sounds heard in the ear are tinnitus aurium Sounds which are vaguely situated in the head are tinnitus cerebri. Sounds of either type are usually heard on one side only and are described variously by the patient.

Tinnitus is a common symptom and may be due to so many conditions that in a given case it is often impossible to determine its cause. Tinnitus is a response of the auditory part of the eighth cranial nerve to abnormal stimuli

It is helpful to bear in mind that the most frequent causes of tinnitus, usually ringing in the ear, as described by the patient, are psychoneurosis with anxiety and consequent vasomotor irregularity, diseases of the ear such as impacted cerumen, otitis with fluid in the middle ear, and obstruction of the eustachian tube; blood diseases, as in anemias and senescence An attack of migraine is frequently preceded by or accompanied with sudden loud noises

Tinnitus with deafness may be due to the administration of quinine, as well as salicylic acid and its compounds Ergot in considerable doses may give rise to ringing in the ears because of its probable action in producing cerebral anemia. Various subjective sounds, due to toxemia, circulatory disturbances or aural disease, may be present in some of the *infections*, particularly cholera, malaria and rickettsial fevers

Tinnitus or ringing in the ear is a symptom of ear disease in 8 out of 10 patients affected with otologic disorder. When tinnitus is associated with an otologic disease, there is always an accompanying deafness, which may be slight, low-pitched, roaring or rumbling, constant or throbbing, or high-pitched, whistling or ringing

Unilateral tinnitus and very severe or total deafness of the perception and nerve type, with or without vomiting and vertigo, followed by numbness in the face, diplopia, occipital-frontal pain, stiffness of the posterior neck muscles, unsteady gait and ataxia, choked optic nerve head, loss of corneal reflex, weakness of the lower part of the face of the same side, with a dead labyrinth on a caloric test and Kernig's sign, are highly suggestive of an expanding intracranial tumor or, if there is fever, a brain abscess.

Vertigo. True vertigo may be caused by labyrinthine disease, lesions of the central nervous system such as acoustic tumor and cerebellar disease. Often the

ing which follows inflammation of the middle ear resulting from simple or specific infectious rhinopharyngitis, postnasal adenoids, enlarged faucial tonsils, nasal polyps, and nasal stenosis from any cause. Wax in the meatus, aural polyps, parotitis or other inflammations and growths may produce deafness by closing the external meatus. A unilateral deafness of sudden onset is often of central origin. During the course of meningococcic meningitis or meningoencephalitis, typhoid fever, influenza, scarlet fever or measles, deafness may occur which follows the destruction of the nerves, the nerve ganglia or the structures of the labyrinth by the meningeal inflammation

With advancing age there is a loss of hearing for high-pitched tones, deafness of the nerve type with tinnitus in one or both ears.

Overuse or hypersensitiveness to quinine and salicylates may cause a degeneration of the nerve cells. The use of these drugs during pregnancy may affect the unborn child through the placental circulation. In lead poisoning the lead may act on the vessels of the cochlea and on the brain Phosphorus, carbon monoxide, chenopodium, arsenic, mercury, morphine and aniline dyes have produced nerve deafness. Streptomycin at times seems to have a specific transitory toxic effect on the cochlea and vestibular branches of the auditory nerve. The deafness and tinnitus caused by streptomycin usually disappear after its discontinuance However, the vestibular effects of the drug often are permanent

Permanent deafness may begin abruptly on the fourth and fifth days of epidemic parotitis (mumps).

Hemorrhage into the labyrinth, if both divisions of the eighth nerve are involved, may produce sudden but permanent deafness and loss of function of the semicircular canal apparatus, since it destroys the essential end-organs.

Traumatic and *occupational deafness* may occur as a result of different forms of acoustic trauma; as a blast injury or prolonged exposure to loud noises. In hysteria and malingering mere pretense of deafness is common.

The distinction between ordinary middle-ear deafness and nerve deafness is made by testing with a watch or a vibrating tuning fork. If the deafness is due to *aural disease*, the ticking of a watch or the vibrations of the tuning fork are heard faintly or not at all when the instrument is held at varying distances from the ear, these noises become distinctly audible when the watch or the handle of the tuning fork is placed in contact with the skull or the mastoid process (bone conduction). The sound is heard best by the nonaffected ear if deafness is due to disease of the auditory passages, by the affected ear if deafness is due to obstruction of the air passages. In *nerve deafness* the watch and the fork are heard indistinctly or not at all, either in contact or at a distance In ordinary deafness the nerve is normal and can appreciate vibrations brought by the bone, but through some fault in the mechanism aerial vibrations are not transmitted to the nerve endings In nerve deafness the nerve is at fault and cannot appreciate vibrations, no matter how well they may be conducted.

The *Weber test* determines whether nonaural impairment is of obstructive or nervous origin by comparing the bone conduction of the two ears by means of a tuning fork.

The *Rinne test* is used to compare the duration of bone conduction with that of air conduction for the ear being tested The patient is Rinne positive when air conduction is greater than bone conduction The patient is Rinne negative when bone conduction is greater than air conduction

Otosclerosis. In otosclerosis there is the formation of new soft bone in the capsule of the labyrinth which replaces the normal bone, with ensuing progressive deafness due to fixation of the footplate of the stapes.

Otosclerosis is a distinct nosologic entity due to a genetic mutation with dominant characters. In the heterozygous state otosclerosis rarely becomes manifest; if it does, it is less severe than in the homozygous state and appears only at advanced age This genetic factor may not be manifest for several generations, but despite this, histologic examination of the organ of hearing reveals the existence of otosclerotic foci.

The clinical manifestations of heterozygous otosclerosis can be influenced by

rhagic or degenerative; to hydrops of the labyrinth; to suppurative or other disease of the middle ear; to a vasomotor disturbance of the vessels of the semicircular canals which may accompany a neurosis, and to disease of the centers of hearing and equilibration.

The vertigo of Ménière's disease is sudden in its onset, and the patient may fall before there is time to prevent it. There may be a transitory loss of consciousness. The face is pale and covered with perspiration Nausea and vomiting ensue. There is present a tinnitus which may consist of hissing, buzzing, roaring or throbbing noises The attacks tend to recur several times in a day, or may be months apart Rare symptoms during the attack are diplopia and nystagmus, double vision, or oscillatory movements of the eyeballs The deafness usually is progressive but incomplete, affecting one or both ears In intervals between the attacks there may be few symptoms, but a continuous giddiness is a common complaint

In those who have symptoms of Ménière's disease a test of the reaction of the vestibular function and the testing of hearing are necessary. The determination of the function of the vestibular portion of the end-organ as it functions through the semicircular canals is obtained through the Bárány test (caloric test)

The value of the caloric test (Bárány's symptom) depends on stimulating the endolymph in the semicircular canals to move. On sudden movement of the endolymph in a normal individual, nystagmus and vertigo ensue The stimulus is effected by turning the subject, or by instilling hot or cold water into the external auditory canal in order to change the temperature of the endolymph

In carrying out the turning test, the subject is turned in a special chair, with head in proper position, at a certain rate of speed and for a definite number of times The caloric test is conducted by instilling cold water (68 F, 20 C) or hot water (112 F, 44.4 C) into the external auditory canal By either the turning or the caloric procedure nystagmus and vertigo of definite types and duration will be produced in normal persons Absence of reactions or change in character of reactions has pathologic significance. Interpretations of the abnormal reactions must be made by those experienced in conducting the test. This test should not be used when the ear drum is perforated

Diagnosis depends on the history and the positive findings as recorded and interpreted

Motion Sickness. The essential cause of motion sickness, for example seasickness, train sickness or air sickness, is the abnormal stimulation of the vestibular apparatus by the unusual motion to which the patient is subjected. Psychic influe[illegible] part in the production of motion sickness. Stimulation of the semi[illegible] symptoms, this occurs, for example, dur[illegible] drops in a down draft The symptoms are [illegible] sometimes diarrhea, with intense headache and mental depre[illegible] the vomiting and diarrhea may produce profound dehydration, and the lack of food intake may cause *acidosis, so that shock ensues.*

Deafness. The hearing mechanism consists of two portions, the conductor and the receptor. The external ear and the middle ear represent the conductor; the internal ear represents the receptor

More instances of deafness result from advancing years than from disease of the tympanic membrane, the middle ear or the eustachian tube. Disease of the auditory nerve, its nucleus, or its cortical center gives origin to nerve deafness Often no cause at all can be found to account for deafness Deafness may be congenital or acquired.

Congenital deafness may result from defects in development of the hearing apparatus as the result of intra-uterine syphilis or German measles or from the administration of quinine to the mother prior to the birth of the child. Congenital deafness often coexists with deaf-mutism

Acquired deafness usually results from loss or impairment of the power of hear-

The color of the eye is not a simple hereditary component. For instance, of blue eyes alone there are 9 shades or classes, which are transmitted in heredity in no less than 45 possible combinations.

The Palpebral Fissure; the Eyelashes and Eyebrows. The breadth or the transverse diameter between the openings of the eyelids is the palpebral fissure. The palpebral fissure varies racially as follows: narrowest in the Mongolian peoples, widest in the whites, and intermediate in the Negroes. The height of the upper lid is classed as low, mid and high. This measurement decreases with age, owing to growth of the facial skeleton and development of the supra-orbital complex.

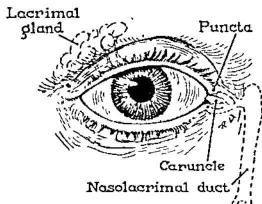


Fig 4-4 Region of the eye

The eyelashes and the eyebrows vary greatly among individuals in appearance and color. They are not always the same color as the hair. In men the color of the beard corresponds with the color of the hair, except that red beards may occur when the hair is dark. Eyelashes and particularly eyebrows add much to the physiognomic effect of the face. In women the eyelashes and eyebrows are so altered cosmetically that descriptions of their natural appearance are nullified Women tweezer off or paint on eyebrows to suit their particular type of beauty. They may glue on false eyelashes

With the advent of middle age a man may be made aware of his years by the barber saying, "Shall I trim the eyebrows, sir?" In other words, a brief description of beginning old age in men is, the time when hair begins to grow where it should not be, and ceases to grow where it should be

Headache of Ocular Origin. Unilateral head pain of ocular origin is common Pain radiating through one eye may be due to a ciliary spasm, localized neuralgia or the spasm of a single ocular muscle A shooting, knifelike, intermittent, stabbing pain, when due to ciliary spasm or a spasm of a single muscle, is associated with the use of the eyes Localized viral disease along nerve trunks may cause prolonged local pain Postneuritic pain may be severe Inflammation of the gasserian ganglion and irritation of the internal carotid artery from aneurysm are uncommon causes of eye pain Glaucoma is often the source of unilateral or bilateral eye pain.

Nearsighted persons do not have headache or head pain unless the nearsightedness is unequal or severe or unless they are abusing their eyes. Abuse in the use of nearsighted eyes may produce severe headache, nausea, and vomiting

Farsighted persons are likely to have frontal headaches which are moderate to severe and are present almost daily in the afternoon or evening. Farsightedness sometimes is definitely associated with certain types of work

If there is an inequality in the amount of error in the two eyes, the pain may be severer over one eye and commoner as a cause of headache.

Errors in refraction usually produce frontal, vertical or bitemporal pain, which may be associated with slight dizziness Nausea is usually relieved by going to bed or resting or taking a single tablet of acetylsalicylic acid. It is made worse by sewing, playing cards and other close application. An error of refraction associated with a muscle error is almost certain to produce symptoms of headache, such as pain or nervousness, irritability, exhaustion, nausea and loss of weight The ophthalmologist is uncertain about a patient's muscle balance if the patient has some constitutional

exogenous factors and also by endogenous milieu. These factors, especially the endogenous milieu, will precipitate the manifestations at an earlier age even in those who have been conditioned for this sort of deafness.

The manifestations consist of a progressive loss of hearing for low tones by air conduction with or without tinnitus There is an apparent improvement of the hearing when exposed to noise (paracusis willisiana). However, the loss of hearing does not vary from day to day except for its progression toward deafness. Eventually there is deafness of a mixed form

The findings on examination depend on the progress of the disease There is present conduction deafness in both ears without a previous history or findings suggestive of otitic suppuration in a patient of less than 30 years of age. The genealogic history reveals that a similar form of deafness may have been present in previous generations. In all, the deafness has progressed more rapidly during gestation or serious illnesses than at other periods. Owing to nerve degeneration there is finally an impairment of hearing of the mixed form

Interpretation of Hearing Tests. Guild has expressed the opinion that nothing is gained clinically by making hearing tests which cannot be interpreted with reasonable certainty in terms of causative lesions In other words, if there be no histologic evidence to support or to refute the diagnostic interpretations customarily made of the data obtained by most of the elaborate, time-consuming technics, in the interpretation of these technics only a description of the kinds of hearing defects found by the tests made and not a diagnosis is given Guild has expressed an opinion that for most patients a few simple tests of hearing afford all the information the clinical otologist needs to supplement or to confirm the impressions gained from the history and the physical examination, and has reached the conclusion that a clear distinction should be made between tests for research purposes and tests for clinical purposes.

The histologic findings in instances of conduction deafness of similar degree as given by Guild lend emphasis to the statements that the practical conclusion is that despite any advances in methods of testing hearing, reliance on the clinical history and the physical examination must continue in order to determine why a patient is hard of hearing and what can or should be done about it

THE EYE

The signs and symptoms referable to the eye are of importance not only from the standpoint of disability from eye disease but also with reference to disorders of the nervous system and in connection with diseases of other organs

The Color of the Eye. The pigment of the eye is contained in the conjunctiva, the sclera, the iris, the choroid, the ciliary processes and the retina The color of the eye ranges from brown through gray and green to blue The lack of pigmentation of the eye in albinism is abnormal but not pathologic The impairment of vision produced by albinism is mainly due to photophobia and nystagmus

There are three major types of distribution of the pigment of the eye the mixed, the rayed and the zoned In the eye of *mixed* colors the periphery of the iris is of some light clear shade, specks or dots or perhaps strands of different color, sometimes variations of the color of the iris, but commonly brown, yellow or orange, encircle the pupil *In the rayed* eye the pigmentation varies in intensity and radiates from the pupil somewhat in the manner of spokes from the hub of a wheel In the *zoned* eye the pigmented part of the iris is a well-defined band around the pupil, the periphery is gray, green, blue or yellowish

In the newborn the eyes are blue or violet As a child grows, the area around the pupil becomes pigmented so that a brown areola and a light background are characteristic. Among European peoples the color of the eyes darkens during adolescence. In general, the coloring of the eyes tends to keep pace with darkening of the hair. In the aged the coloring of the eyes decreases and the eyes appear faded.

Ectropion. Ectropion is an eversion of the eyelid with exposure of the conjunctival surface of the lids; it may affect both lids. The condition is secondary to scarring of the lids However, it does occur in the aged as a part of the relaxation of the skin and the orbicularis oculi muscle. Atrophy may occur with ectropion as a part of an affection of the facial nerves, causing paralysis of the orbicularis oculi muscle, and under these circumstances the ectropion is known as the paralytic atrophic type. This affects only the lower lid

Trichiasis. Trichiasis is an inversion or ingrowing of eyelashes so that they rub against the cornea. This condition is manifested by congestion of the cornea, pain, lacrimation, photophobia, opacities, vascularization and ulceration. The most common cause of trichiasis is chronic trachoma.

Swelling, Puffiness. The eyelids, particularly the lower, are swollen in general anasarca, and are often the earliest seat of edema of renal origin. Anemia and hypoproteinemia may be attended by swelling of the lids. A bloated appearance of the eye, possibly with ecchymoses, is common in severe cough and pertussis. Angioneurotic edema and phenomena indicative of the allergic state may be seen in this locality. Edema of the lids and forehead which occasionally occurs in neurotic and adolescent individuals is often of allergic origin

Because of the anatomic connection between the blood vessels of the face and those of the cranial cavity, cerebral thrombosis may give rise to a swelling of one or both eyelids, with some protrusion of the eyeball, the puffiness subsequently extending to the face. Likewise infections of the face may extend through these same vessels and produce thrombosis of the cerebral venous sinuses.

Erysipelas and the stings of insects may be the cause of swelling so great as to prevent opening of the eye Severe coryza, hay fever, arsenic poisoning and iodism may induce noticeable swelling of the lids So, also, the lids are swollen in measles, variola, varicella and rickettsial infections, to mention only a few causes for swollen lids.

Hordeolum (Sty) A small, painful abscess at the edge of the eyelids is a sty or hordeolum When sties occur in successive series, it may be indicative of the overuse of defective eyes Small, single, and superficial sties are of purely local origin A sty is to be differentiated from chalazion (cyst of a meibomian gland), a slow-growing tumor which may become inflamed and suppurate.

A cystic swelling, of some duration, toward the inner canthus is a *mucocele* (chronic dacryocystitis), which may become inflamed and suppurate. After measles, scarlet fever, ophthalmia or other diseases in which there is conjunctival inflammation, there may be an acute inflammation of the lacrimal sac.

Ankyloblepharon. Ankyloblepharon is an adhesion of the margins of the upper and lower lids It may be either a congenital condition or due to burns. It may be partial or complete, and is often combined with symblepharon as a part of widespread scarring and deformities of the eyelids

Blepharophimosis. Blepharophimosis is a contraction of the palpebral fissure at the outer canthus. The outer angle is obscured by a vertical fold of skin from contraction following prolonged epiphora and blepharospasm.

Blepharospasm. Blepharospasm is characterized by an increased winking of the eyes Essential blepharospasm is the normal amount of winking of the eyes, both lids moving synchronously. Symptomatic blepharospasm may accompany disease of the eye as of the trigeminus nerve.

The term blepharospasm also may designate a slight narrowing of the palpebral aperture which may be of congenital origin or form ankyloblepharon.

Lagophthalmos. Lagophthalmos is a condition of incomplete closure of the palpebral aperture when the eyes are shut It may be due to narrowing of the lids from contraction of a scar, or to congenital deformity, ectropion, paralysis or loss of power of the orbicularis oculi, facial paralysis, or proptosis due to orbital tumor or

disease such as hyperthyroidism, hypothyroidism, paralysis agitans, encephalitis or diabetes.

There is a definite seasonal and periodic increase in head pain originating in the ocular muscles. Such headaches become more frequent in October, reach a peak in January and fall off in the spring. These headaches may be related to inactivity for when the days become longer and outdoor exercise is resumed, the incidence decreases.

The child who has a nervous breakdown or who is inattentive, the adult who has a headache at noon which is relieved by lunch and then has a recurrence at about 3 or 4 P.M., the student who cannot concentrate, and the convalescent patient who has headache may belong to the group of persons who have faulty, poor or inadequate ocular musculature. It is common to observe instability of eye musculature in patients undergoing a period of physical debility. Many of these patients who have ocular muscle imbalance are unaware of their difficulty.

Those who have hyperthyroidism, hypothyroidism and other glandular disturbances producing headaches often have been given a pair of glasses during the acute stage of the general disease. When recovery was attained, the tone of the ocular muscles improved and then the glasses were not suitable for them.

THE EYELIDS

The skin of the lids is thin and the subcutaneous tissue loose and devoid of fat. For these reasons after injury blood finds its way readily into the lids and shows plainly beneath the skin, as in the familiar black eye.

Mongoloid Fold. The mongoloid fold occurs commonly among Mongolians and occasionally among the whites.

The epicanthal fold among the Chinese, for instance, is, on the whole, much thicker than among white peoples. This condition of thickening in the Chinese eyelid is due to a characteristic disposition of the lower part of the orbicularis oculi muscle plate whereby, as seen in sagittal sections, the lower marginal fibers are disposed backward in a curve or even a kink.

Coloration of Skin of the Eyelids. A darkening or *duskiness* of the lids and under the eye is seen in some women and men. Duskiness in either men or women may be prominent in the anemia and pallor of brunet persons, or after fatigue, mental excitement, loss of sleep, or severe pain, and in exhausting diseases. Dark circles around or under the eyes are often hereditary and have no other significance. This condition is chiefly an affection of brunets who have thin fair skin.

One or more soft and very slightly elevated yellow patches seen on the upper eyelids of middle-aged women, or of elderly men or women, but most frequently in the soft tissue below the lower lids, are manifestations of xanthelasma. These spots or plaques, varying in size from 1 mm. to 1 cm. in diameter, when on the eyelid are situated near the inner angle, they may be either unilateral or bilateral. They may extend to, or primarily involve, the skin under the lower lid. These are of no diagnostic significance.

Coloboma of the lid is a triangular notching of the upper lid at the junction of its inner and middle thirds. Damage may be done to the eye if the deformity is not corrected.

Tophi. As in the ear, so may small nodules of sodium urate, significant of gout, form in the eyelids.

Entropion. Entropion is a rolling in of the margins of the eyelids and eyelashes. It is observed when there are scars or spasms of the lids. Cicatrical entropion most commonly affects the upper lid. Spastic entropion, which is due to spasm of the palpebral portion of the orbicularis oculi muscle, almost always affects the lower lid. These conditions are manifested by mechanical irritation and injury to the cornea from the turned-in eyelashes. There are congestion, pain, lacrimation and photophobia. If not corrected, opacity, vascularization and ulceration of the cornea ensue.

Carcinoma of the lid is usually a basal cell epithelioma, which is termed rodent ulcer. Malignant tumors of the eyelids occur in older people and more frequently on the margin of the lower than of the upper lid.

The tumor begins as a small elevation in the epithelium which ulcerates early and appears as an ulcer with indurated edges. The ulcer slowly spreads. Highly malignant squamous cell epithelioma occasionally occurs in young persons and spreads rapidly to the adjacent lymph nodes along the sides of the neck.

Sarcomas are rarely present on eyelids.

THE LACRIMAL APPARATUS

The lacrimal gland consists of two portions, an orbital or superior portion and a palpebral or inferior portion. The lacrimal gland opens by several fine ducts into the fornix of the conjunctiva.

The lacrimal canal, embracing the sac and the nasolacrimal duct, each about 12 mm in length, extends from just above the internal tarsal ligament or tendo oculi to the inferior meatus of the nose Below the palpebral ligament the sac is comparatively weak, and here it is that distention occurs and pus makes its exit

Dryness and Moisture of the Eye. The eye may become *dry* and *glazed* in prolonged fevers as well as in disease attended by lagophthalmos.

Lacrimation, an increased secretion of watery fluid, usually accompanies irritation or inflammation of the conjunctiva, and accordingly is present in measles, influenza, pertussis, and rickettsial infections in the early stages; in hay fever, asthma, coryza, trifacial neuralgia, facial paralysis and iodism, and when a foreign body is present in the eye The tears may overflow the edge of the lids (epiphora) because of displacement of the puncta lacrimalia or obstruction of the duct Cold winds and irritating vapors stimulate the flow of tears

Hyposecretion of lacrimal fluid is manifested by a feeling of dryness and burning, smarting sensation in the eyes, photophobia, and impairment of the vision Hyposecretion or deficiency in lacrimal secretion does result from extirpation of the lacrimal gland but is usually caused from the scarring of the conjunctiva that follows trachoma and xerophthalmia.

Stagnation of the contents of the lacrimal sac is quickly followed by infection and inflammation and is termed dacryocystitis. The lacrimal sac may become obstructed by either congenital causes or diseases of prenatal influences, or as a result of chronic nasal infection

Reduced production of lacrimal fluid is found in a condition known as keratoconjunctivitis sicca, often associated with defective secretion of the salivary gland and arthritis In vitamin A deficiency dry, greasy areas, known as Bitot's spots, may develop on the bulbar conjunctiva in the interpalpebral space

Epiphora is an overflow of tears and is a symptom in affections of the tear-conducting apparatus. The common causes of epiphora are exposure to wind or smoke, affections of the nose, and irritation of the retina by bright light It may also be dependent on increased secretion, which occurs in facial paralysis or from affections of the ophthalmic branch of the trigeminus nerve due to foreign bodies and inflammation of the eye Epiphora is commonest in old people, especially those who are exposed to the open air in cold weather, and often is without manifest lesions of the conjunctiva or tear passages

The ophthalmologist investigates the lacrimal passages by digital or instrumental pressure over the lacrimal sac and by injection of physiologic saline solution through the inferior punctum with the lacrimal syringe. If on pressure over the lacrimal sac a watery, viscid, mucopurulent discharge escapes through the punctum, it indicates an obstruction of the nasolacrimal duct. When obstruction is present, it may be situated in the nasolacrimal duct, or in the lacrimal sac, or at the junction of the common canaliculus with the lacrimal sac.

to exopthalmic goiter. In the last-named disease lagophthalmos is conjoined with protrusion of the eyeball (proptosis) and inability to follow with the upper lid a downward movement of the eyeball (von Graefe's sign) Lagophthalmos may be due to laxity of the tissues and absence of reflex blinking in patients who are extremely ill or moribund. Incomplete closure of the lids during sleep is commonly present in exhausting diseases. As the eyeballs are normally turned upward in sleeping, the scleras are thus exposed, giving a ghastly expression to the face. Owing to exposure the cornea becomes epidermoid (*xerosis corneae*) or keratosis sets in.

A similar rolling up of the eyes and imperfect closing of the lids are frequently seen in hysteria, in various convulsive disorders during the convulsion and immediately after death See ptosis (fall) of the upper lid, page 120.

Blepharitis. Blepharitis is characterized by reddened, thick, inflamed and crusted edges of the eyelids The edge of the lids may possibly be affected by minute ulcers or pustules The condition often results from an allergy, a previous ophthalmia or an attack of measles, or it may accompany anemia. Often, however, the cause is unknown.

Blepharitis is often the source of a chronic conjunctivitis. The etiology of the conjunctivitis may be suggested by the appearance of the blepharitis For instance, a mixed bacterial infection is often irregular in distribution and omits the meibomian glands and follicles of the cilia, whereas the staphylococcal variety involves these structures.

Residual swelling from recurrent sties indicates a residual staphylococcal infection of the lid margins which may be the source of a chronic conjunctivitis.

Meibomianitis is often present in conjunctivitis Expression of the contents of the meibomian glands and observation of the expressed material are regularly a part of the examination of the edges of the eyelids when disease is suspected. An inflammatory enlargement of one of the meibomian glands is termed *chalazion*

Swelling, redness and dilatation of lacrimal puncta are characteristic of streptomycotic concretions, which constitute an important cause of unilateral conjunctivitis. The diagnosis can be made by expressing material from the punctum and detecting the streptomyces on microscopic examination or on cultures

Molluscum contagiosum is a contagious disease caused by a filtrable virus The incubation period is variable, from 14 to 50 days It is transmitted by direct contact Man is the only known host The virus is cosmopolitan in distribution and affects all ages. The disease is characterized by the formation of firm, rounded, pearly white *skin nodules or tubercles varying in size from one to several millimeters in diameter* The lesions appear on the eyelids, the face, the scalp, arms, legs, buttocks, mucous membranes of the mouth and genitalia as single or multiple nodules. The soles and the palms are never affected These nodules usually present a central depression and contain semifluid caseous matter or solid matter made up of fat, epidermis and peculiar capsulated bodies, the molluscum corpuscles

Chronic edema of the eyelids due to blockage of lymph vessels is a characteristic feature of *lymphogranuloma inguinale keratoconjunctivitis* and can be considered almost pathognomonic of the infection

Herpes zoster ophthalmicus is an involvement of the eyelid when there is herpes zoster of the ophthalmic division of the fifth nerve The lid is affected by the characteristic lesions of herpes zoster The pain is severe The lesions heal, leaving scars which may be disfiguring

Tumors. *Papillomas* of the eyelids are common along the edges of the lids. They should be removed. Papillomas also include the verruca or wart Xanthelasma, naevus, hemangioma and lymphangioma may be present on the eyelids.

Small cysts having transparent contents are due to obstruction of the outlets of sweat glands, or keratomalacia, and are often seen on the borders of the eyelid. They give rise at times to irritation

which accompanies diphtheria; membranous conjunctivitis, however, may be non-diphtheritic. Meningitis may cause inflammation and discharge, perhaps unilateral, similar to that caused by the gonococcus.

Conjunctivitis may be a serious manifestation of tularemia (see Chapter 17).

The viral infections, for instance, acute coryza (head colds), influenza, measles, yellow fever and smallpox, often have conjunctival manifestations. The rickettsial diseases all affect the conjunctivae.

Purulent conjunctivitis, or ophthalmia neonatorum, is usually caused by the gonococcus. This is an extremely severe form of conjunctivitis and in the newborn child is a potent cause of blindness if not immediately treated by silver nitrate drops in the eyes

Gonorrheal conjunctivitis in the adult is acquired by direct transfer of material infected with gonococci to the eye. The usual method of transfer is by the hands from the genitals The unusual transfers occur from the use of soiled towels or spattering of pus containing the organisms. The incubation period is from a few hours to 2 or 3 days

The disease varies in severity. In the virulent infections the eyelids may begin to swell and within a few hours become so tense that they cannot be opened. In all there is a rapidly developing chemosis. The lids and fornix of the affected eye are swollen, tense and covered with a profuse purulent secretion. In severe infections there may be only a blood-tinged discharge. In a few days the symptoms begin to subside but the eye continues to discharge pus for 2 to 3 weeks. The course as well as the disease has changed greatly since the advent of chemotherapy and antibiotic therapy

Untreated or inadequately treated gonorrheal conjunctivitis often injures the cornea—corneal ulceration. Ulceration is followed by cicatrization, staphyloma and sometimes a panophthalmitis

The diagnosis of gonorrheal conjunctivitis is usually obvious from the history One eye alone is affected. In the mild forms of the disease the diagnosis may be difficult because of resemblance of the disease to other forms of acute bacterial conjunctivitis and viral conjunctivitis, particularly swimming-pool or inclusion conjunctivitis The diagnosis is made from positive smears and cultures

The subjective symptoms of acute conjunctivitis are itching and smarting sensations, usually referred to the eyelids These sensations become progressively more intense and the lids feel hot and heavy as though sand or foreign bodies were underneath the lids There is a varying amount of photophobia Owing to altered secretions on the cornea, there may be blurring of the vision. The symptoms are usually worse toward evening than during the rest of the day The affection may be limited to one eye, but usually both eyes are implicated; either from the start, or within a very few days after the first eye is affected, the other will become involved.

All types of infectious conjunctivitis are characterized by the brilliant red color of the conjunctiva due to hyperemia and formation of new vessels When the upper lid alone is reddened, the possible presence of a foreign body is a first consideration.

The various types of *allergic conjunctivitis* are common and can often be distinguished by the character of the conjunctival secretions. The secretion from allergic conjunctivitis, particularly vernal catarrh, has a high fibrin content and is stringy in character in contrast to the flaky or amorphous exudate of an ordinary bacterial infection.

drops. Full or excessive doses of many drugs such as arsenic, potassium iodide and sulfonamides, especially if there is an idiosyncrasy, cause chemosis.

Obstruction of the *nasolacrimal ducts* may be due to prenatal influence or may be the result of chronic nasal infection, trauma or ulceration, or may occur idiopathically Obstruction of the nasolacrimal ducts is manifested by epiphora at all times but is greatly increased by exposure to cold, wind, dust or smoke.

Acute inflammation of the lacrimal gland is a rare condition. The gland is sometimes enlarged in mumps or epidemic parotitis. A bilateral enlargement of the lacrimal glands is rare *Dacryocystitis,* infection of the lacrimal system, may become chronic and produce a form of chronic conjunctivitis affecting chiefly the upper lid Occasionally a blepharitis accompanies these conditions. Acute exacerbations of a chronic form of dacryocystitis may be manifested by acute swelling and obstruction resulting in abscess formation in the lacrimal sac

In *eversion of the puncta* the lower punctum looks forward and away from the depression where the tears accumulate and thus epiphora results. Eversion of the punctum and the canaliculus may be of congenital origin or it may be caused by scarring from wounds or by chronic inflammation. This condition most commonly occurs in old age or in facial palsy, conjunctivitis, blepharitis or ectropion The canaliculus may contain a cilium or concretions which irregularly obstruct the passages and produce a swelling of the tissue at the inner canthus of the eye

Malignant tumors of the lacrimal ducts and glands of the eye occur and these are usually sarcoma These tumors are classed with orbital tumors The most frequent orbital tumors are those that extend into the orbit from the adjacent structures, usually from the meninges or the brain They may extend from the zygomatic and temporal fossae or from the nasal cavities When such infiltrations occur, the eye is protruded and dry.

Dermoid tumors arising from remnants of the orbital crest occur at the outer or inner angles of the eyes, more frequently at the outer angles Dermoid tumors are to be differentiated from meningoceles

THE CONJUNCTIVA

The conjunctiva lines the eyelids (palpebral conjunctiva) and covers the eyeball (bulbar or ocular conjunctiva) in front.

A *symblepharon* is a cicatricial attachment between the conjunctiva of the lid and the eyeball It is usually caused by an injury.

A *pterygium* is a triangular fold of membrane occupying the interpalpebral fissure extending from the inner or outer part of the ocular conjunctiva to the cornea. This condition occurs usually in elderly people who have lived in the wind and dust of the plains or deserts

Subconjunctival hemorrhage or ecchymosis often occurs without assignable cause. Occurring after an injury, either form of bleeding may indicate a fracture of the base of the skull anteriorly, the blood passing forward into the orbit The other causes are the violent straining which may occur in severe coughing, severe vomiting, straining at the time of bowel movements and heavy lifting. *Subconjunctival ecchymoses* may also occur during a convulsive seizure and in asthma or severe dyspnea. They may be hemorrhagic infarcts and significant of septicemia or septicopyemia

Conjunctivitis or inflammation of the conjunctiva is common and often is caused by the presence of foreign bodies in the eye or by exposure to wind, either hot or cold, and to dust or pollens, smoke or intense light.

The infectious forms of conjunctivitis due to bacteria may be acquired from [illegible] Epi-
[illegible] ies
[illegible] ac-
terial origin, is often known as *pink-eye* and is likely to occur during the spring or fall months (vernal conjunctivitis). Conjunctivitis may be of the membranous type

the lower lid. On re-

tivitis the *second eye* becomes involved after a varying period of time. As a rule, the course of the disease in the second eye is much shorter and the inflammation considerably less than in the first eye.

Systemic manifestations are headache and night pain, fever and malaise which may occur with involvement of the one or the second eye. Corneal involvement is a frequent and serious complication, and this may occur without any signs of pain or photophobia or other subjective or objective symptoms. The intensity and sequence of appearance of the symptoms therefore have no bearing on the duration or intensity of the disease. Often eyes which show violent symptoms in the beginning may clear up rapidly and without resultant visual impairment. The time interval between the onset of the disease and the involvement of the cornea varies from 1 to 5 weeks. Usually the first sign of corneal involvement is the appearance of several tiny punctate infiltrates of the cornea in the subepithelial layer The corneal epithelium remains intact and does not stain with fluorescein In the majority of cases the corneal infiltrates are on the exposed part of the cornea, that is, within the confines of the palpebral fissure, and usually in the pupillary area.

The diagnosis of epidemic keratoconjunctivitis depends on the presence of an acute keratoconjunctivitis with practically no discharge from the conjunctiva. This stage is followed by an acute swelling of the preauricular nodes and in some there is also swelling of the submaxillary and cervical nodes.

Herpetic Keratoconjunctivitis. The clinical characteristics which should arouse suspicion of an herpetic etiology in any inflammatory condition of the eye were outlined by Maumenee, Hayes and Hartman as follows: (1) the frequency with which it follows pyrexia; (2) relapses or recurrences; (3) slight, if any, purulent discharges; (4) herpetic vesicles on the lids; (5) bacteriologic sterility of the conjunctiva, (6) rapid and complete healing as a rule, (7) hypesthesia of the eye, (8) a visible and slightly tender preauricular node Many of these clinical manifestations can be caused by the virus of epidemic keratoconjunctivitis

Inclusion Conjunctivitis (*Paratrachoma or Swimming Pool Conjunctivitis*) This disease is caused by a virus of large particulate size belonging to the psittacosis-lymphogranuloma venereum group of organisms The conjunctivae are increased greatly in thickness and contain numerous basophilic cytoplasmic inclusion bodies which are morphologically identical with those of trachoma. The disease occurs in infants and in adults

The incubation period is from 5 to 12 days In the infant the disease develops rapidly, particularly in the lower lid, and pseudomembranes may develop rapidly. After 10 to 15 days the disease decreases in intensity, but it lasts for months or for a year

In the adult the disease develops as a follicular conjunctivitis with scanty discharge and periauricular adenopathy. As in the disease in infants, the lower lid is more severely involved than the upper lid The disease in the adult is more chronic than that seen in the infant

The diagnosis of inclusion conjunctivitis in the infant is made most easily by remembering that this conjunctivitis is likely to commence 5 to 12 days after birth, whereas gonorrheal conjunctivitis begins very soon after birth The lower fornix has a coxcomb-like appearance, and inclusion bodies can be demonstrated. Trachoma never occurs in the newborn child.

In the adult, diagnostically significant is the presence of inclusion bodies from the lower lid in a patient who does not have pannus or significant conjunctival cicatrization The follicular hypertrophy is much more definite in the lower lid than in the upper.

Ulcers of the cornea are attended with reddening of the eye. Characteristically, glaucoma may cause reddening of the conjunctivae.

Facial paralysis, by causing undue exposure of the eyeball or a neuralgia of the fifth nerve, may give rise to redness and inflammation

Follicles are not visible on the normal tarsal conjunctiva. When follicles are visible, they have hypertrophied. The significance of *follicular hypertrophy* depends primarily on location and secondarily on their prominence. Follicles involving the upper tarsal conjunctiva are suggestive of trachoma When the upper tarsal conjunctiva is clear and follicles in other parts of the conjunctivae are affected the diagnosis usually is follicular conjunctivitis. The follicles of trachoma are soft, gelatinous and easily expressed, while the follicles of follicular conjunctivitis are hard and expressible only with difficulty

In a true *membranous conjunctivitis*, coagulation of the fibrinous exudate has occurred so that removal of the membrane leaves a bleeding, rough surface. Conjunctival *pseudomembranes* are of two types, the fine, transient type and the thick, relatively permanent type An example of a fine, transparent membrane occurs in vernal catarrh, acute conjunctivitis such as gonococcal conjunctivitis and epidemic keratoconjunctivitis

Thick, opaque, pseudomembranes occur in diphtheria, in streptococcal infections, in erythema multiforme, and occasionally in ocular pemphigus

Conjunctival ulceration is characteristic of conjunctival tuberculosis and oculoglandular tularemia, chancre of the conjunctiva and acute pemphigus The ulcers of acute pemphigus are readily distinguished from other ulcers by their shallow character and transient nature

The conjunctival *phlyctenule* or an elevated nodule or an ulcer of the corneal conjunctiva is pathognomonic of phlyctenular conjunctivitis and is believed to be an allergic reaction to a bacterial antigen, commonly tuberculoprotein Unlike conjunctival phlyctenules, corneal phlyctenules lack diagnostic value

Conjunctival granulomas are associated with buried foreign bodies or ruptured chalazia, conjunctival tuberculosis and oculoglandular tularemia The conjunctivae in leptothrichosis have small, whitish or grayish necrotic foci without gross ulceration A single large granuloma without diffuse conjunctival inflammation is suggestive of rhinosporidiosis

Conjunctival concretions indicate the occurrence of past or present chronic conjunctivitis Their diagnostic value is slight, but when they occur in large numbers *they can be considered suggestive of an old trachoma*

Conjunctival *scars* follow injury, operation for chalazia or burns, trachoma, pemphigus, diphtheria and irradiation The scars of trachoma involve the upper tarsal conjunctiva predominantly and those of ocular pemphigus the lower tarsal conjunctiva and fornix Ocular pemphigus may cause an obliteration of the entire lower fornix, a condition which distinguishes it from trachoma

The term *superficial punctate keratitis* is a descriptive name of epidemic keratoconjunctivitis, and it is often employed as a general morphologic term for the designation of any condition presenting multiple, small, discrete lesions of the cornea affecting the epithelial and immediately adjacent subepithelial tissues.

Epidemic Keratoconjunctivitis. This is a disease of viral origin There is evidence to indicate a close immunologic relationship between the viruses of epidemic keratoconjunctivitis and St Louis, Japanese and West Nile encephalitis viruses.

The earliest symptoms vary greatly in intensity. They commence with a sandy feeling, redness and swelling of the palpebral conjunctiva of *one eye*. At this stage it may be thought that there is a foreign body present causing tearing of the eye. After 12 to 36 hours the bulbar conjunctiva too becomes congested and hyperemic, and varying degrees of edema of the lids (particularly of the upper lid) ensue Occasionally the amount of edema is extreme and it may be difficult to open the eyes

be present along the lower retrotarsal fold without any evidence of inflammation, and as such the condition is known as *folliculosis*

THE CORNEA

The cornea is the transparent portion of the external coat of the eyeball, the anterior extension of the sclera The cornea consists of four layers. (1) the corneal epithelium, which is continuous with that of the conjunctiva; (2) the substantia propria; (3) the posterior elastic lamina and (4) the endothelium of the anterior chamber of the eye. The last three layers anteriorly are continuous with similar tissues of the sclera However, in the sclera there is not the definite arrangement of tissues as in the cornea. In contrast to the cornea, the outer surface of the sclera is bluish white and nontransparent.

Diseases of the Cornea. Many of the inflammatory diseases of the cornea have been discussed in connection with inflammation of the conjunctiva, which is continued over the cornea Injuries of the cornea have been included with other injuries of the anterior part of the eye.

Ulcers. A reddened, painful, photophobic eye, with a clear cornea, except for a loss of substance at one point, is an example of a corneal ulcer. Corneal ulcerations often result from scratches or foreign bodies, conjunctivitis and burns of the eyes. Exophthalmos, unilateral from a tumor of the orbit, or as a progressive condition of unknown cause, but usually associated with exophthalmic goiter, may be the cause of corneal ulceration The ulcerations in exophthalmic goiter, and also in some cases of facial paralysis, may be due to the constant exposure of the eye consequent on the inability of the lids to cover the protruding eyeballs.

The unilateral inflammation of the eye in meningitis may lead to a corneal ulcer. In disease of the first division of the fifth nerve, for instance herpes zoster with or without resulting anesthesia of the cornea and conjunctiva, the cornea may undergo ulceration, occasionally intractable.

Hypopyon is a collection of pus in the anterior chamber of the eye, which may accompany corneal ulceration. The pus is derived, not from the corneal ulcers, but from an exudation from the iris and the ciliary body when these parts participate in the inflammation

Opacities of the Cornea. Opacities of the cornea are usually caused by corneal ulceration or involvement of the cornea by inflammation or ulceration as the result of an injury. An opacity of the cornea will reduce vision when it encroaches on the pupillary area Over the pupillary area a very slight opacity may cause much visual disturbance on account of the resulting diffusion and irregular refraction of light A linear or a nebular form of opacity will cause a great deal more visual disturbance than a circumscribed opacity Dense opacities or deformities of the cornea may cause a disfigurement of the eye as well as interfere with its vision

Interstitial or deep keratitis is characterized by a cellular infiltration of the deep layers of the cornea without ulceration during any stage of its existence There is involvement of the uvea which accounts for many of the symptoms

In many instances the disease is due to *congenital syphilis* It affects girls and boys alike and becomes manifest between the ages of 5 and 15 years In rare instances the patient may be older

During the early stages of congenital lues there are successive periods of photophobia, lacrimation, pain, and interference with vision in both eyes In some instances the symptoms subside and the eye clears up entirely or nearly so

In the beginning, there is present a patch of grayish infiltration which may be situated in any part of the cornea The patch enlarges to involve the entire front of the eye The cornea becomes softened The blood vessels begin to appear over the periphery of the dull gray-appearing cornea, giving the limbus a reddened color. Vision may be reduced to light perception only. However, improvement will usually take place eventually.

In both infants and adults the disease resolves without residual conjunctival or corneal changes

Trachoma. Trachoma is caused by a filtrable virus. The virus of trachoma is *distinctive from most other viruses, since it seems to be susceptible to chemotherapy,* to originate basophilic intrusion bodies and to have an intercellular cycle of morphologic variation For these and other reasons it has been suggested that trachoma and inclusion conjunctivitis should be classified with the rickettsial diseases. An objection to such a classification is that trachoma is not transmitted by an arthropod host.

Trachoma is a highly contagious disease, which is responsible for much partial or total blindness. The disease may present few or no symptoms. The onset of the disease usually is with a mild conjunctivitis with thickening, edema, and congestion of the conjunctivae In some patients there are photophobia, blepharospasm, lacrimation, itching, burning, and painful sensations accompanied by visual disturbances.

On examination in the early stages of the disease there may be found minute follicles which can be seen in the upper tarsal conjunctiva On microscopic examination of the scrapings from these follicles, the characteristic inclusion bodies may be found At this stage it is difficult to differentiate trachoma from inclusion conjunctivitis or gonorrheal conjunctivitis As the disease progresses, there is papillary hypertrophy of the tarsal conjunctiva, especially of the upper lid, which imparts to the lid the characteristic granular appearance With further progression the papillae may increase in size, and there appears a diffuse infiltration of the conjunctiva, which is studded with grayish, rounded, translucent follicles arranged in parallel rows. The trachomatous pannus consists of loops of blood vessels extending into the cornea between the epithelium and Bowman's membrane, these loops are caused by a stopping or cutting off of the blood vessels by scarring The cornea presents a cloudy appearance and may be gray and translucent. Its surface becomes vascularized, the blood vessels stringing from the conjunctival vessels at the limbus. This process advances until it covers the upper half of the cornea In severe cases it may cover the entire cornea and thus vision and perception of light are reduced and the patient loses his eyesight

From this stage of development of trachoma the disease may continue to progress, or complete retrogression may take place, so that the cornea again becomes *transparent The final visual condition depends on the extent of corneal opacification* and unevenness In severe instances of the disease iritis develops which is due to a change similar to those which occur in the conjunctivae Superficial corneal ulcers may appear near the margin of the advancing iritic pannus Ptosis may develop and become permanent

Trachoma, after months or years, reaches the stage at which formation of scar tissue is the predominating process As scar tissue forms, the papillae and the follicles disappear In the tarsal conjunctiva there may have formed narrow bands of white scars which parallel the lid margin In general, trachoma heals by the formation of scar tissue Consequently the sequelae are as follows. ectropion, entropion, *or trichiasis Often the movements of the eyeballs are restricted,* iritic pannus may be present, and corneal opacities may result from the corneal ulcers. Staphyloma of the cornea may follow a perforation of a corneal ulcer A dry, scaly state of the conjunctiva may be a sequela of severe trachoma

The diagnosis is made from the prolonged course and on the basis of the clinical examination and the finding of characteristic minute inclusion bodies in the cytoplasm of epithelial cells in scrapings from the conjunctiva

Chronic Conjunctivitis. Any of the acute forms of conjunctivitis may be followed by chronic conjunctivitis, the symptoms of which are essentially a prolongation of an acute form of the disease *Follicular conjunctivitis* is a form characterized by the occurrence of lymph follicles distributed along the lower retrotarsal fold. They appear as small, round, oval, pinkish bodies arranged in rows These follicles may

mortar or whitewash, strong acids and alkalies endanger the eye by injuring the cornea and producing symblepharon. Strong ammonia is particularly harmful, causing necrosis of the cornea; hydrochloric acid much less so. The central core of golf balls often contains caustics such as barium sulfate or sodium hydroxide which spurt into the eye if the ball is slit open

Ensuing immediately on the introduction of a caustic into the eye are intense conjunctivitis and chemosis, but the cornea looks clear; in this stage it is difficult to be certain of the extent of the injury. A drop of fluorescein solution in the eye will reveal on magnification the extent of the area denuded of epithelium. Therefore the patient is urged to secure the services of an ophthalmologist until the gravity of the injury can be determined. In severe injuries the cornea is dull or opaque. In the succeeding days an eschar forms and is thrown off This is followed by granulation of the injured conjunctiva and frequently by ulceration of the cornea. In severe burns the foregoing process may cause the whole cornea to be destroyed; perforation takes place, and the eye shrinks In less severe burns a dense milky white opacity forms, porcelain-like in lime burns, and sight is lost There is little danger of the loss of sight in the less severe injuries but the conjunctiva may form adhesions of the lid to the globe Adhesions are most likely to occur with the lower lid, the caustic acting principally on the lower fornix, which is obliterated by organization of the granulation tissue. The symblepharon thus produced impedes the movements of the globe and may even interfere with its nutrition

THE ORBIT

Pain In and Around the Eye. Foreign bodies and inflammatory diseases of the iris or conjunctiva are common causes of a painful eye. Pain in and around the eye is frequently due to trigeminal neuralgia or to migraine. Before treatment is given, these conditions should be differentiated from acute glaucoma to avoid error in therapy The presence of dimmed vision, reddened eye, hazy cornea, dilated pupil and greatly increased tension, perhaps with nausea and vomiting, will declare the case to be one of glaucoma.

Photophobia is a form of eye pain excited by exposure to light. It is present to varying degrees in the conjunctivitis of measles, influenza, the early stage of pertussis and severe coryza, or the formation of the vesicles of variola and varicella on the cornea Ocular or retinal hyperesthesia is a rare form of photophobia not dependent on local inflammatory disease of the eye, and it is usually, although not always, due to functional disturbance of the optic tract and nerve or the cortical centers for vision It is a frequent *symptom in neurasthenia, hysteria, migraine and*, at times, the hypnotic state. It may be present in cinchonism, in the early stages of [illegible]

[illegible]

[illegible] the orbital tissues (panophthalmia).

Suppuration of the orbit may originate extrinsically and extend into it as from erysipelas, from caries of the orbital bones or adjacent structures or in syphilis. If pus enters the orbit, it is usually from suppuration of the frontal sinus and ethmoidal cells. If so, the swelling presents at the upper portion of the inner angle of the eye. Pus in the maxillary sinus usually discharges into the nose. Pus within the orbit [illegible]

[illegible]

[illegible] orbital tumors, however, arise extrinsic to the orbit and enter through its natural openings or extend directly through its bony walls. Tumors arriving in the orbit through natural openings may enter (1) from the brain through the optic foramen or sphenoidal fissure, (2) from the region of the zygomatic and temporal fossae

In some instances all of the signs of the disease disappear. In others, when there is severe involvement of the iris, choroid and vitreous, sight may be lost or there may remain a permanent opacity in the cornea.

The diagnosis of interstitial keratitis of syphilitic origin is based on the history The physical examination often reveals the presence of Hutchinson's teeth, scars at the angles of the mouth where rhagades have healed, and head deformities. The head deformities consist of a square forehead and prominent frontal eminences Often there are enlarged lymph nodes in the posterior triangles of the neck. There may be visible tibial deformities. The roentgenographic examination of the bones may reveal irregular cortical outlines.

The classic triad for the diagnosis of congenital syphilis is (1) interstitial keratitis, (2) Hutchinson's teeth and (3) deafness (labyrinthine disease).

Arcus Senilis. This is a degenerative condition of the cornea. The true arcus is an ill-defined, grayish, partial or complete ring at the circumference of the cornea, the cornea itself being somewhat hazy It was formerly wrongly considered to be an indication of beginning arteriosclerosis and the degeneration of old age. The false arcus is a sharply delineated ring of a clear yellow or yellowish white color, due to a deposit of fat Neither one is of diagnostic significance.

INJURIES TO THE ANTERIOR STRUCTURES OF THE EYE FROM FOREIGN BODIES AND PHYSICAL AGENTS

The eye is subject to injury from foreign bodies, burns, the action of caustics, contusions, wounds and radiant energy

Foreign Bodies. Foreign bodies on the conjunctiva or on the cornea cause sudden discomfort and blepharospasm The foreign body may adhere to the palpebral conjunctiva, or it is likely to be dragged across the cornea, which it excoriates. It may be floated by tears toward the inner canthus and pass into the nasal duct. Very frequently it becomes lodged at about the middle of the upper sulcus subtarsalis, where it is likely to irritate the cornea, or in the upper fornix. When it adheres to the bulbar conjunctiva, it may lodge there Foreign bodies are generally imbedded in a mass of granulation tissue The chitin of insects and the husks of seeds may adhere to the cornea, usually at the limbus, for several days or even weeks or until the inflammatory reaction is sufficient to dislodge them

Particles of steel and emery are likely to penetrate the epithelium or substantia propria. Larger particles of steel, stone or glass may perforate the globe. When situated in the cornea, they cause great pain and irritation The pupil is often constricted If allowed to remain, they expose the cornea to the dangers of infection by organisms in the conjunctival sac and ulceration This may lead to a small superficial slough being cast off, carrying the foreign body with it The small ulcer thus formed may heal, but if virulent organisms are present, a spreading ulcer, with or without hypopyon, may develop

Foreign bodies are probably more frequent in the lower cul-de-sac than in the upper, but in the former location they may be removed by the lacrimal fluid or by the patient's own efforts The upper cul-de-sac requires more scrutiny than does the lower, for it extends several millimeters above the tarsus in the upper lid, and simple eversion of the upper lid may not expose it. When a foreign body is suspected but remains undetected, the tarsus should be everted and then the cul-de-sac stretched forward and convexly with a lid everter The fold behind the lacrimal caruncle is another recess which may conceal a foreign body.

Intra-ocular foreign bodies are suspected in blast injuries, or when the patient has been near the application of striking, grinding or cutting force applied to metal.

Burns and Injuries by Caustics. Burns by hot water, steam, hot ashes, exploding powder or molten metal, and injuries by caustics such as lime, usually from fresh

if toward the nose, the strabismus is convergent or internal. Vertical squint may be upward or downward. By asking the patient to look at the tip of the examiner's finger, it is usually easy to decide which eye squints and whether the squint is convergent, divergent, upward, or downward If the strabismus is slight and uncertainty arises, the finger should be held directly in front of the face, about 18 inches (46 cm) distant, and the patient asked to gaze at it The apparently normal eye should then be covered by a card. The uncovered eye, if it be the squinting one, will immediately alter its position so as to fix itself on the finger, thus demonstrating that it had not before been properly directed.

Strabismus, with reference to its origin, may be of two kinds, concomitant and paralytic.

In *concomitant strabismus* the squinting eye will retain its mobility, moving readily in every direction concomitantly with its companion, the degree of strabismus remaining substantially the same. The principal causes of concomitant strabismus are overaction of certain muscles consequent on refractive errors, and imperfect vision of an eye, with resulting weakness of the muscles.

In *paralytic strabismus* the squinting eye loses some of its power of movement, owing to a loss of power in one or more of the external ocular muscles. Closely connected with and dependent on paralysis of the ocular muscles and strabismus is the subjective symptom of diplopia.

DIPLOPIA. Double vision depends on the fact that unless the visual axes are correctly adjusted, each to the other, the images of the objects do not fall on identical points in the retinas. Under normal conditions each image falls on the macula lutea of each retina, combining to form a single image in the sensorium

Aside from the double vision which is produced by the action of alcohol, atropine and other drugs on the ocular nerves, diplopia, like strabismus, is a symptom of paralysis of the ocular muscles Any lesion of the brain, spinal cord or basal meninges which causes paralysis of one or more of the external ocular muscles may be attended with diplopia.

Double sight with one eye may occur in cataract and astigmatism, owing to irregular refraction, and in brain tumor as a psychic aberration

CONJUGATE DEVIATION. If both eyes are turned strongly and persistently toward one side, either right or left, the condition is termed conjugate deviation This condition may be due to either spasm or paralysis of the internal rectus of one side and the external rectus of the other side, and the eyes may be turned toward the lesion or away from it, depending on its location and whether it is irritative or destructive This symptom depends on the normally associated action of the internal rectus of one side and the external rectus of the other in effecting horizontal co-ordinated motion of both eyes to the right or left

The lesions producing conjugate deviation are, in particular, cerebral hemorrhage, thrombosis, tumors and meningitis Often, if the lesion is a left-sided one and causes right hemiplegia, the eyes look toward the lesion, but it is said that if the lesion is irritant or becomes so and spasms or convulsions occur, the eyes turn away from the lesion

The determination of the nature of the lesion must be made by study of the associated symptoms of brain tumor, meningitis, apoplexy, sclerosis or abscess.

NYSTAGMUS. This is a rapid involuntary oscillation or slow movement of both eyeballs, usually from side to side (lateral nystagmus), sometimes vertical or rotary. It is a clonic bilateral spasm of the ocular muscles due to some irritation, either functional or organic, affecting the ocular muscle centers. If nystagmus is very slight, it may be intensified by directing the patient to look steadily at an object held well to one side or the other, or if the nystagmus is vertical or rotary, by directing the eye upward or downward, or circumducting the eye by moving the object

Nystagmus is present in many cases of blindness or defective sight caused by

through the sphenomaxillary fissure or (3) from the nasal cavities through the nasolacrimal duct.

Tumors which arrive in the orbit by penetrating its walls may come (1) from the nasal cavities and ethmoidal cells, pushing through the thin internal wall; (2) from the frontal sinus, appearing at the upper inner angle; (3) from the sphenoidal cells at the posterior portion of the inner wall; (4) from the brain cavity above, breaking through the roof, or (5) from the maxillary sinus below, pushing through the floor.

Dermoids and Meningoceles. In the fetus the frontonasal process extends to join the maxillary processes on each side This leaves an orbitonasal cleft to form the orbit Owing to defects in the development of this cleft, dermoid tumors may occur in its course They are seen at either the outer or the inner angle of the eye They are commoner at the outer angle near the external angular process than at the inner angle, and may have a prolongation to the dura mater They also occur at the inner angle at the frontonasal suture. At this point, also, meningoceles are likely to occur

Symptoms Indicative of Disturbances of the Ocular Muscles. PTOSIS Drooping of the upper eyelid, with inability to raise it (ptosis), may exist alone, but it may be combined with paralysis of the third nerve Ptosis is usually due to paralysis of the levator palpebrae As the levator palpebrae is innervated by the second portion of the oculomotor nucleus, ptosis is dependent on some interference with the function of the third nerve, its nucleus, or its cortical center

Ptosis may be congenital and hereditary, unilateral or bilateral, partial or complete In complete ptosis the lid drops enough to interfere with vision. The attempts made to counteract this interference with vision consist of throwing the head back and raising the eyebrows by forced contraction of the frontalis muscle Instances of partial ptosis may be masked by these compensatory mechanisms Detection of partial ptosis is accomplished by asking the patient to look upward while the eyelashes are pressed firmly against the inferior bony margin of the orbit

Berke classified congenital ptosis in accordance with the muscles or structures involved, separating them according to whether the superior rectus muscles are involved alone or there is weakness of the superior rectus and the inferior oblique muscles combined In addition to involvement of the recti and inferior oblique muscles attention is paid to ptosis associated with the jaw-winking phenomenon and, finally, to ptosis that may be associated with blepharophimosis Congenital ptosis is most frequently unilateral This classification of congenital ptosis is useful, since it is helpful in selecting the proper surgical procedure if any is to be employed

Acquired ptosis is usually unilateral It may be part of the symptom complex of paresis or paralysis of the whole of the third nerve, or may be due to paresis or paralysis of the branch supplying the levator Isolated ptosis without other signs of oculomotor paralysis may result from disease of the brain (cerebral ptosis) Acquired ptosis may be due to direct injury of the muscle or its nerve supply, deformity and increased weight of the lid brought about by edema, trachoma, and tumors. In inflammatory necrotic processes and during marasmus with tissue loss the lid may sag from lack of support Bilateral ptosis may occur as a part of the syndrome of myasthenia gravis In severe neuralgia of the fifth nerve in tetanus, in autonomic nerve lesions and in hysteria, ptosis may coexist

The amount of ptosis sometimes alters with the position of the globe, attaining its highest pitch in abduction of the eye, its least in adduction. In all forms of ptosis there may be a synkinesis of movement, the lid rises when the jaw is moved, as in mastication, though it remains immobile when an attempt is made to look upward

STRABISMUS. Squint or strabismus is inability to bring the visual axis of both eyes to bear at the same instant on one point, the visual axis of one eye constantly deviating, as a rule horizontally, sometimes vertically, from the object inspected If the squinting eye turns toward the temple, the strabismus is divergent or external;

lid from paralysis of the levator palpebrae, and dilatation of the pupil and paralysis of the accommodations of the eye If the sixth or abducens nerve is paralyzed, the eye cannot be turned outward. If the fourth or patheticus nerve is paralyzed, the superior oblique muscle fails to act, and the double vision produced is worse when the patient looks down because the superior oblique is normally a depressor muscle. The lacrimal, frontal and nasal branches of the fifth nerve are nerves of sensation, hence in supraorbital neuralgia and that affecting the nasal branch, pain is felt in the orbit at the inner angle of the eye and down the side of the nose

Ocular Paralysis. Paralysis of the ocular muscles is termed ophthalmoplegia. In testing the ocular muscles for evidence of paralysis or weakness ask the patient to follow the finger moved in different directions. Evidences of weakness or paralysis may thus be detected when there is inability of the eye to follow the moving finger If a more careful investigation is needed, as with the slighter degrees of paralysis and the ocular asthenopias, the patient should be referred to a competent ophthalmologist.

Paralysis of the Third Nerve. If there are ptosis, slight exophthalmos, external strabismus, diplopia, and a dilated pupil which reacts neither to light nor to accommodation, and if when an object is moved in various directions the eye fails to follow it upward, inward, or far downward, but will move outward and a little downward by means of the external rectus and superior oblique, there is complete oculomotor paralysis. In many cases some of the muscles escape, the levator and rectus superior or the iris and the ciliary muscle being alone affected, or ptosis may exist, with a dilated pupil

The most frequent causes of oculomotor paralysis are exposure to cold and to syphilis, the latter giving rise to a basal meningitis or a gummatous growth involving the roots of the nerve Various forms and degrees of oculomotor paralysis are significant symptoms in cases of encephalitis and botulism

Partial paralysis may be due to a cortical lesion affecting the inferior parietal lobule. Undue exposure to light, migraine, and the excessive use of alcohol or morphine may cause temporary paralysis

As organic disease of the third-nerve nucleus is usually associated with disease of the fourth and sixth nuclei, an oculomotor paralysis, without loss of power of the external rectus and superior oblique, is, as a rule, functional.

While the nerve is penetrating the crus it may be involved by tumor or other lesion of the crus, in which case there will be partial or complete third-nerve paralysis conjoined with hemiplegia on the opposite side of the body, a combination characteristic of unilateral disease of the crus If in addition there are unilateral paralysis and atrophy of the tongue, the lesion is localized in the inner and inferior aspect of the crus involving the cerebral fibers passing to the nucleus of the hypoglossal or motor nerve of the tongue.

Ptosis occurring on one side, disappearing and then appearing on the other side (alternating), may be due to variable lesions in the neighborhood of the nucleus.

At and after its emergence from the pons on its way to the sphenoidal fissure, the third nerve may be involved by basilar meningitis or tumors

The lesions of locomotor ataxia which cause ptosis may be in the same locality. If due to disease at the base, the oculomotor paralysis is usually bilateral and likely to be accompanied by interference with the function of the other cranial nerves Third-nerve paralysis may also be one of the symptoms of primary muscular atrophy and upper bulbar palsy

Oculomotor paralysis may be indicative of pressure in the cavernous sinus or inflammation at the sphenoidal fissure, or injury (fracture) in either locality

Loss of accommodation, loss of light reflex, and external squint following an attack of diphtheria are usually indicative of a neuritis of the third nerve

Paralysis of the Fourth Nerve. The fourth nerve supplies the superior oblique muscle, and paralysis of this muscle is somewhat difficult of detection If paralyzed, when the fixing object is moved downward below the horizontal line the diseased eye fails to follow it, there is slight convergent strabismus, and the patient has double vision while looking down.

optic atrophy, amaurosis, and corneal opacities. It may be found in albinos. It is frequently seen in epileptic or other convulsions, and may form a part of the symptomatology of neurasthenia, hysteria, chorea and, in some cases, of multiple sclerosis and insanity

The most important diagnostic associations of nystagmus, however, are with Friedreich's ataxia, disseminated (insular) multiple sclerosis, and brain tumor, especially growths involving the cerebellum, pons or crus Acute basal meningitis is likely to present nystagmus.

A special variety of nystagmus may be inherited. It resembles in appearance the ocular type, yet it is not associated with defective vision. The movements of the eyes are constant, horizontal and pendular, of small range on forward gaze and of increasing amplitude on gaze to the sides. The rate is about 120 per minute. In most cases it is noted by the mother when the child is a few weeks to a few months of age.

This type of nystagmus, according to Rucker, is usually a sex-linked character, the gene being carried on the X chromosome In some families hereditary nystagmus is transmitted on an autosome In some this type of nystagmus is associated with red-green color blindness

IRREGULAR OR SPASMODIC MOVEMENTS OF THE EYES Nonrhythmic, irregular movements of the eyes may occur in connection with special ocular paralyses or insufficiencies and errors of refraction. Ménière's disease, when due to lesions of the labyrinth, is sometimes accompanied by forced movements of the eyes. Chronic hydrocephalus and meningitis (basal irritation) may give rise to irregular spasmodic movements of the eyeballs In hysteria the internal rectus and levator palpebrae may be tonically contracted, the eyes being opened, convergently squinted and uprolled.

Asthenopia and Insufficiencies of the Ocular Muscles. If complaint is made that close use of the eyes, such as that involved in writing, reading, or sewing, causes them to feel strained, hot, and uncomfortable, and perhaps gives rise to headache in the forehead, vertex, or occiput, the source of the trouble may be found in a weakness of the ocular muscles, particularly the recti If this weakness exists, the patient cannot keep the visual axes of the eyes in proper relation without an effort, either conscious or unconscious.

If normal strength of the ocular muscles is present, the condition is called *orthophoria*. If some of the muscles are weak, it is termed *heterophoria*

The varieties of heterophoria are. *esophoria*, weakness of the externi, causing a tendency to convergence of the visual axes, *exophoria*, a tendency to divergence of the visual axes from weakness of the interni, *hyperphoria*, a tendency of the visual axis of an eye to deviate upward, *hypophoria*, the tendency of the visual axes to deviate downward

None of these deviations is sufficiently obvious to constitute strabismus. All of these conditions require the advice of an ophthalmologist after he has examined the patient.

The consensus among those trained in ophthalmology and neurology appears to be that the importance of muscular asthenopia in causing various forms of nervous disease has been greatly overrated. According to the more conservative view, muscular asthenopia is not a factor in causing nervous disorders, but in neuropathic individuals it may intensify or render more frequent attacks of migraine, trigeminal neuralgia, occipital and cervical headaches, vertigo, and perhaps choreiform movements of the upper facial muscles The correction of refractive errors and the wearing of glasses may relieve the troublesome symptoms

Nerves of the Orbit. The optic nerve is the nerve of sight. Interference with it produces blindness. This nerve will be discussed separately later in the text.

The oculomotor or third nerve supplies all the muscles of the orbit except the external rectus and superior oblique. If the third nerve is paralyzed, the eye cannot be moved upward, inward, or to any extent downward. There will be ptosis of the upper

The observations which may be made on examining the eyeball relate to pulsations in and around the eye, the protrusion or recession of the eye, its position and its degree of mobility.

Visible pulsation of the eyeball may be found in aortic insufficiency, arteriovenous aneurysm, great cardiac hypertrophy, and vasomotor instability, as in exophthalmic goiter and other conditions in which there is abnormal throbbing of the arteries.

Protrusion. Exophthalmos of a moderate degree is commonly of congenital origin. Protrusion of the eyeball, when bilateral, has as its commonest explanation exophthalmic goiter. The eyes may protrude in asthma or other conditions attended by severe dyspnea. Thrombosis of the superior longitudinal sinus may be attended by unilateral or bilateral protrusion of the eyeball and swelling of the face

Swellings or tumors may displace the eyeballs forward, usually on one side, perhaps on both sides, as in great enlargement of the lacrimal gland and arteriovenous aneurysm, exostosis, cancer of the orbit, or tumors of the upper maxilla. One or both eyes may be pushed downward and forward and come to rest in the upper portion of the orbit by subperiosteal hemorrhages which may be present as one of the lesions of scurvy.

Instruments to measure the protrusion of the eye have been devised, the best known of which is the Hertel exophthalmometer, a satisfactory instrument though somewhat difficult to use. A simpler instrument is the one devised by Luedde, but since the position of the two eyes is not measured at the same time it requires great care to be sure that the instrument is similarly placed on each side in turn The normal reading with the Hertel instrument seems to be about 15 mm , but it is variable.

The protrusion differs with different causes In a general overfilling of the orbit by increase in its contents the eye projects straight forward and can move in every direction This is the condition seen in exophthalmic goiter A tumor within the muscle cone, if not too large, produces the same effect, but a large tumor in the cone tends to move and displaces the eyeball to the side. Tumors in the orbit outside the muscle cone push the eye to one side

Malignant exophthalmos occurs in association with exophthalmic goiter. The exophthalmos may increase despite relief from the toxic symptoms. It has been postulated that this condition is due to a hormone different from the one which causes exophthalmic goiter

Various theories have been propounded to explain the development of exophthalmos by local reasons It has been variously attributed to an increase in the orbital fat, to edema of the normal orbital contents, to congestion of the vascular bed of the orbit, to relaxation and hypertrophic myositis of the extra-ocular muscles, and to contraction of the smooth muscles Exophthalmos may follow paralysis of the ocular sympathetic nerves (see Autonomic Nervous System, Chapter 23).

The malignant type of exophthalmos most commonly occurs in patients aged 40 years or more The sex incidence is almost reversed from that of the incidence of exophthalmic goiter Men are therefore more commonly affected than women. Once a progressive or malignant exophthalmos is established, rarely does a complete regression of the exophthalmos occur The condition may become stationary, or it may progress until disorganization of the eyeball is so great that excision of the globe has to be performed It is now generally accepted that there is an edema of all the orbital tissues outside the globe, and this increase in size of the orbital contents pushes the eyeball forward. It also restricts the free movements of the eyeballs.

Unilateral Exophthalmos. Unilateral exophthalmos occurs as a nonpulsating and as a pulsating form

The most frequent causes of a *nonpulsating unilateral exophthalmos* are retrobulbar tumors of soft tissues, bony orbital tumors or vascular lesions such as varicocele of the ophthalmic veins. Infections of the sinuses, soft tissues and bones

The diplopia is an extremely annoying symptom, as the eye is so constantly employed in writing, reading, and walking, all of these occupations requiring down turning of the eye The head is likely to be carried forward and toward the sound side.

Isolated paralysis of the fourth nerve is very infrequent. When present, it may be indicative of pressure on the nerve trunk as it winds around the outer surface of the crus to reach the anterolateral edge of the pons

The coexistence of symptoms of cerebellar disease with fourth-nerve palsy is indicative of a lesion of the anterior part of the cerebellar hemisphere on the same side. There may be paralysis of the fourth nerve, presumably due to a peripheral neuritis as the result of epidemic influenza, diabetes, alcoholism, lead poisoning and tumor However, such paralysis may be a transient symptom of myasthenia gravis.

Sixth Nerve. A lesion of the nucleus of the sixth nerve may cause conjugate deviation of the paralytic form.

Third, Fourth, and Sixth Nerves. Total ophthalmoplegia may be indicative of disease in the cavernous sinus of the sphenoidal fissure, especially if there is anesthesia of the peripheral distribution of the ophthalmic division of the trigeminal nerve (skin of forehead, upper eyelid and nose) The branches of this division accompany the ocular nerves through the sphenoidal foramen, and they may be involved by lesions in these localities, that is, syphilitic or other periostitis, gumma or other tumor, aneurysm or arteriovenous aneurysm of the internal carotid, or thrombosis of the cavernous sinus

Ophthalmoplegia, external, internal or total, may be a symptom of acute or chronic polioencephalitis superior (upper palsy, nuclear palsy), or encephalitis or botulism

When paralysis of all the ocular muscles is associated with facial paralysis without hemiplegia, it is probably due to a basal lesion, since the facial nerve, like the ocular nerves, is liable to involvement by disease at the base

DIAGNOSIS OF MULTIPLE OCULAR MUSCLE PARALYSES The diagnosis of paralysis of a single ocular muscle may be difficult on occasion When more than one muscle in the same eye is paralytic, a much more difficult task is encountered, and if one or more muscles in each eye are paralyzed, the signs can be confusing, owing to all degrees of paresis of the muscles, and innervational overaction and underaction, spasm, contractures and fibrosis of other muscles not involved It can be safely said that only experienced ophthalmologists are aware of the difficulties that sometimes attend the analysis of ocular muscle paralysis

The ophthalmologist employs the Maddox rods, screen test, test of rotations or ductions, test of versions, test of diplopia fields, past pointing, and head tilting in his diagnostic procedures

Immediately after paralysis is acquired, all the characteristic symptoms and signs, such as diplopia, limitation of motion, primary and secondary deviation, false orientation and the subjective sensations of vertigo and dizziness may be present. As the paralytic condition continues, the original symptoms become modified, diplopia becomes less obtrusive, compensatory head tilting becomes apparent, fixation may change, and unopposed or innervationally overacting muscles may become spastic and undergo contraction with fibrosis The originally nonconcomitant strabismus gradually takes on the characteristics of a concomitant disturbance. The complexity of this transition is multiplied by the simultaneous paralysis of two or more muscles.

POSITIONS OF THE EYEBALL

The positions of the eyeball in its socket are classed as flat, midprominent, or protruding With age the increasing relaxation of the extra-ocular muscles causes the eyes to appear flat or less deeply imbedded than in early life. This change is less marked in women than in men.

of the wound become yellow and necrotic, hypopyon appears, there is chemosis, with intense ciliary and conjunctival congestion, and the lids are swollen and red. The vitreous becomes purulent, as shown by a yellow reflex by oblique illumination. The anterior chamber soon becomes full of pus, and the cornea cloudy and yellow; ring infiltration may occur. There may be exophthalmos and limitation of movement of the globe, due to extension of the inflammation. In the early stages of metastatic panophthalmia rapid failure of vision, a yellow reflex, and hypopyon are found.

If the disease is permitted to take its course, the sclera is ruptured, usually just behind the limbus. The pain subsides, and after prolonged suppuration the eyeball shrinks and vision is lost. Sympathetic ophthalmia is unlikely.

As soon as it is evident that the eye cannot be saved it should be excised.

Sympathetic Ophthalmia. Sympathetic ophthalmia is a rare condition in which serious inflammation attacks the sound eye after injury of the other eye. The disease is thought to arise from an infection.

Sympathetic ophthalmia almost always is caused by a foreign body which remains within the eye without suppuration. Wounds involving the iris, ciliary body or lens capsule without suppuration are likely to set up sympathetic ophthalmia. Perforating ulcers very rarely cause it

Children are particularly susceptible, but the disease occurs at any age. It usually begins 4 to 8 weeks after the injury to the first eye (the exciting eye) has taken place, rarely earlier, but the onset may be delayed for many months or even years.

The manifestations in the second or sympathizing eye are almost always a plastic iridocyclitis, in rare instances a neuroretinitis or choroiditis In other cases the patient first seeks advice for defective vision or inflammation in the uninjured eye (sympathetic irritation)

The symptoms commence with sensitiveness to light and transient indistinctness of objects. Objects become blurred, if the eye is fatigued, but after an interval of rest vision improves When fully developed, all the symptoms of iridocyclitis are present, varying in degree according to the severity of the disease The prognosis as to vision is always doubtful, but if there is much deposition of plastic exudates in the pupillary area, it becomes extremely grave

On examination at this stage there may be lacrimation, slight ciliary injection, tenderness of the eyeball, as shown by the patient shrinking from an attempt at examination, precipitates on the back of the cornea, and vitreous opacities These early symptoms may occur in intermittent attacks, and spread over a considerable period As the disease progresses, the signs of iridocyclitis are present

The treatment of sympathetic ophthalmia is one of the most difficult problems in ophthalmology and often demands the exercise of superior judgment on the part of the ophthalmologist When restoration of sight is doubtful, the eyeball may have to be sacrificed if treatment fails

INJURIES OF THE EYEBALL

Wounds of the conjunctiva, as has been said, are common. They usually heal readily Polypoid masses of granulation tissue sometimes form on the surface during the healing process. A wound of the lens may escape notice at first, especially if the wound is small Later the wound is made evident by the ensuing corneal opacity.

Small wounds of the cornea limited to the center heal well unless they become infected When infections supervene, a permanent dense opacity is left, and the contraction of the organizing scar tissue may cause an irregular astigmatism.

The danger of corneal opacities is greatly increased by a large wound of the eye if it extends into the sclera, or if the lens is also wounded. In the larger wounds of the sclera, prolapse of the iris is almost certain to occur. A physician should never yield to the temptation to replace a prolapsed iris even if this is possible since it may carry infection into the eye. It must be excised.

of the orbit may produce an exophthalmos. Prominence of the eye may occur as a result of an anterior staphyloma or a high myopia.

In the majority of instances *pulsating exophthalmos* is unilateral. The condition usually follows trauma and is the result of a fistula between the internal carotid artery and the cavernous sinus. In some instances a fracture through the base of the skull involving the body of the sphenoid may be demonstrated. Spontaneous instances may occur from rupture of the artery within the sinus, caused by arteriosclerotic plaques, miliary septic aneurysms or congenital weakness of the vessel wall.

The internal carotid artery lies within and is entirely surrounded by a venous channel This arrangement may permit the formation of arteriovenous fistulas with a minimum of trauma The pulsating exophthalmos resulting from an arteriovenous fistula in the cavernous sinus is due to a sudden engorgement of the venous space with arterial blood under high pressure There is a retrograde flow into the ophthalmic veins, with transmitted arterial pulsations and a venous engorgement of the orbital contents and eyelids These changes may occur to a less degree on the opposite side as a result of communications between the two cavernous sinuses.

The diagnosis of unilateral exophthalmos is usually easy, depending on the degree of proptosis Pulsation does not always exist in those cases which occur spontaneously. Following head injuries a bruit, thrill and pulsation usually are present There are headache, disturbance in vision and intracranial noises. The sounds may vary from minor sensations to an almost continuous roaring. The visual field may show a wide range of disturbance. Diplopia may result from an increase in internal or extra-ocular pressures. The presence of chemosis accounts for some of these changes. Blindness may be due to atrophy of the optic nerve, to glaucoma or to cataract

The extrinsic movements of the eye are limited by the proptosis and the alterations in the nerve mechanism of the extra-ocular muscles The retinal findings are not constant and depend on the duration of symptoms. Compression of the common carotid artery will result in a cessation of a bruit, thrill and pulsation when present. Arteriograms may be obtained by the injection of thorium dioxide into the carotid arteries This procedure is useful in diagnosis in obscure cases The radioactivity of this or similar substances should limit its use.

Recession. Enophthalmos, or sinking of the eyeball into the orbit, if bilateral, may be due to absorption of the cushion fat of the orbital cavity such as takes place in prolonged and continued fevers and in cachexias from any cause. It is notably present during severe dehydration and shock It may also be present in consequence of a rapid and exhausting drain on the body fluids, as in cholera, severe diarrhea and large hemorrhages In collapse it may be due to a deficient orbital blood supply.

INFECTIONS OF THE EYEBALL

Panophthalmia. Exogenous and endogenous forms of panophthalmia are recognized. *Exogenous panophthalmia* is generally caused by infected wounds, whether accidental or the result of operations, and by ulcers. The vitreous is usually first affected; organisms grow in it, and purulent cyclitis, retinitis, and choroiditis result. In most instances the deeper parts of the vitreous become infected

Endogenous panophthalmia arises during the course of septicemias or pyemias The small or the larger arteries in the eyeball may become occluded by septic emboli.

The pneumococcus often is responsible for panophthalmia, but the disease may be caused by staphylococci, streptococci, *Escherichia coli*, *Pseudomonas aeruginosa*, *Clostridium perfringens*, and by saprophytic organisms such as *Bacillus subtilis*

In both exogenous and endogenous forms there is fever (temperature 102 to 103 F), headache, drowsiness, and sometimes vomiting There is severe pain in the eye, due at first to iritis, later to increased tension In the exogenous forms the edges

has been done to vision and unless the process of removal will almost inevitably destroy sight Magnetizable foreign bodies are more easily removed than others if the small or the large electromagnet is available.

If the reaction in the eye does not subside in the course of a week or 10 days, as shown by diminution of ciliary injection and cessation of photophobia and lacrimation, the ophthalmologists may advise removal of the eye In the interval the cornea is examined each day by oblique illumination and magnification in search for precipitates. The presence of these is a more definite indication for excision of the eye.

In the presence of considerable prolapse of vitreous as well as of iris and ciliary body, or if the lens is wounded, there is little probability of saving the eye. If it is almost certain that useful vision will be lost, the risks of sympathetic ophthalmia should not be run and the ophthalmologists will advise prompt excision of the eye.

GLAUCOMA

Glaucoma is a disease accompanied by increased intra-ocular tension which results in hardness of the eye, atrophy of the retina, cupping of the optic disk, and blindness. It is supposed to be due to interference with the drainage of the eye and the circulation of the aqueous humor. Glaucoma may be acquired, may occur in families, or may occur sporadically. Glaucoma of acquired origin as a rule is a disease of advanced life. The familial glaucoma occurs usually before the age of 40 years Instances of sporadic glaucoma too may affect middle-aged persons The cause of the disease often is not known Perhaps the most definite thing recognized in its etiology is that there often is a hereditary tendency The disease tends to occur in hyperopic eyes; myopic eyes are far less liable to the disease but they are not entirely exempt There are a number of varieties of glaucoma distinguished by varying symptoms

Acute glaucoma usually is preceded by a number of transitory attacks, during which there is diminution in the acuteness of vision The sight appears to be obscured as by a fog The patient sees a ring or a rainbow of tints around lights.

The cornea, especially in its center, will often show some congestion, that is, it has a clouded appearance There is a feeling of dullness or slight pain in the eyes and head The pupil is dilated and sluggish in action, and the tension of the globe is slightly to moderately increased.

The *acute glaucomatous attack* commences suddenly and violently in one eye during the early hours of the morning. The constitutional disturbance may be so great that the patient is prostrated, with an irregular, intermittent pulse, pallid face and cold extremities.

The pain radiates throughout the entire head and is most intense in the trigeminal nerve Its acute onset, even though associated with nausea, differentiates glaucoma from intracranial conditions The pain is due primarily to pressure on the ciliary nerve and ciliary plexus

Edema of the eyelids is often present. Lacrimation is an important finding, especially in the absence of any external cause, and is primarily due to reflex irritation. In acute inflammatory glaucoma, as contrasted with chronic compensated glaucoma, the increase of intra-ocular pressure is readily determined by palpation

In severe attacks of glaucoma the entire bulbar conjunctiva and sclera present engorged and dilated vessels so uniform that the color is a deep red This congestion is primarily a venous stasis from the increased intra-ocular pressure In some cases minute hemorrhages may be seen

The cornea presents a steamy appearance. Later the epithelium becomes elevated and is edematous The underlying stroma is edematous and is more or less translucent Edema is followed by vesicle formation involving the superficial epithelium

In an attack of inflammatory glaucoma the anterior chamber is shallow. After the iris comes in contact with the posterior surface of the cornea, adhesions rapidly

Occasionally in perforating wounds pyogenic organisms are carried into the eye and cause rapid dissolution of the cornea and panophthalmia. As the result of the panophthalmia the whole of the central part of the cornea is cast off. The infecting organism has generally been found to be *Pseudomonas aeruginosa* (*Bacillus pyocyaneus*).

Wounds of the corneosclera are particularly likely to originate sympathetic ophthalmia.

When perforation of the sclera has occurred, there is reduction in the intra-ocular tension. If the perforation is near the cornea, the anterior chamber is shallow or obliterated. If the wound is large, prolapse of some of the contents of the globe occurs The uvea is easily recognized on account of its pigmentation since the uvea is the iris, ciliary body and choroid, considered together. Very often the gelatinous vitreous can be seen hanging out of the wound. Blood in the anterior chamber and vitreous hemorrhage may be present with or without perforation.

An eye containing a foreign body is likely to be affected by sympathetic ophthalmia When there is present a perforating wound of the eye, it may be difficult to be sure that it does not contain a foreign body. The foreign bodies most likely to penetrate the eye and be retained are slivers of steel, lead, stone and particles of glass Parts or all of copper percussion caps and, less frequently, spicules of wood may penetrate the eye.

A foreign body large enough to be seen by the unaided eye will cause so much damage that the eye may have to be removed Very small particles which penetrate the cornea or sclera and lodge in the deeper parts of the eye are revealed by roentgenographic study. Most intra-ocular foreign bodies are composed of metallic fragments and are thus radiopaque With the exception of glass containing lead in its manufacture, glass does not cast a shadow on the roentgenogram

Depending on the nature of the foreign body, the pathologic condition set up in the eye is profound and varied. For instance, copper causes suppuration of tissues and a leukocytosis even in the absence of pyogenic organisms. This is due to the peculiar chemical irritation of copper Copper in the lens, however, may cause little reaction because the lens is destitute of active blood circulation. Metals other than iron and copper—for instance, lead, zinc, gold and silver—appear to cause little chemical reaction and usually remain quiescent

The foreign body may pass through the cornea or the sclera and originate minimal symptoms If it has passed through the cornea, the wound or scar can be found by examination with oblique illumination and magnification.

A very small foreign body may be retained in the lower part of the anterior chamber and be hidden by the hemispheric shape of the sclera Glass is particularly difficult to locate in the anterior chamber because its refractive index differs so little from that of the surrounding medium

When a foreign body passes into or through the lens, a traumatic cataract is produced which undergoes the usual changes. A hole in the iris is of great diagnostic significance, for it indicates, usually, a perforation by a foreign body. The foreign body may be visible in the lens, either before or after dilatation of the pupil. It is possible for a foreign body to pass through the iris and through the circumlental space without wounding the lens

A foreign body retained in the vitreous or retina when the lens is clear, and there has been little hemorrhage, may be seen ophthalmoscopically. Often the foreign body can be located by the track it leaves through the vitreous. The track is indicated by a gray line The foreign body, generally black, and often with a metallic luster, is surrounded by white exudate and red blood clot. If the particle has been long in the eye, it may have become encapsulated. Particles more than 1 to 2 mm. in size are almost certain to lead to the destruction of the eye

All foreign bodies should be removed by an ophthalmologist unless little damage

perforation may occur relatively early along the perivascular spaces of the ciliary vessels The orbital tissues then become infiltrated. The lymph nodes are not affected; metastasis occurs mainly to the liver but may be present elsewhere. The first manifestations of metastatic sarcoma of the eye may appear months or years after the eye has been removed and may be revealed by enlargement of the liver and by jaundice

Sarcoma of the choroid appears in persons between the ages of 40 and 60 years. It is always primary and involves one eye only.

The symptoms commence with a defect in the field and diminution in sight depending on the exact seat of the tumor. As the tumor enlarges, there is pain in the eye The symptoms are produced more quickly when the tumor is near the macula than when it is peripheral, since vision is affected early. In other cases the tumor has usually attained a considerable size, and the patients may seek treatment for relief of the pain of glaucoma

The cause of the glaucoma is obscure; in some cases it is due to the lens and iris being forced forward, so that the angle of the anterior chamber becomes blocked. In other instances, particularly those of rapid onset, obstruction to the venous outflow from the eye is the probable explanation, the tumor being in some instances so situated as to press on the venous outlet.

On examination sarcoma of the choroid may resemble in its manifestation a primary detachment of the retina or glaucoma. From primary glaucoma, sarcoma of the choroid is distinguished by the fact that sight is involved before the inflammatory symptoms appear, there are no prodromal symptoms such as usually precede glaucoma nor remissions in symptoms, one eye only is involved, the characteristic field of vision in glaucoma is not present, and the unaffected eye presents no symptoms of glaucoma If the detachment of the retina is extensive, differential diagnosis may be difficult; under such circumstances, the eye will be blind

Secondary carcinoma of the choroid occurs sometimes in late stages of scirrhous carcinoma of the breast, more rarely in cancer of other organs.

THE COATS OF THE EYEBALL

The outer strong fibrous coat of the eyeball is the sclera (sclerotic). The vascular middle coat is the choroid The retina or inner coat is the end-organ of sight and is but an extension of the optic nerve (Fig 4-5).

The sclera forms a firm protective covering or case for the delicate retina within. It is continued forward over the front of the eye as the cornea It is essentially a strong membrane which provides protection The common diseases of sclera and cornea are those of weakness If the cornea weakens, it bulges forward and the protrusion is called an *anterior staphyloma* If the posterior part bulges toward the orbit, a *posterior staphyloma* is formed

The cornea has no blood vessels, but from its exposed position it becomes inflamed (keratitis) and ulcerated, and eventually blood vessels may develop into it from its periphery, constituting the vascularization known as pannus The affections of the cornea have been considered earlier.

The weakest portion of this covering for the eyeball is at the junction of the sclera with the cornea On this account blows on the eye cause it to rupture, usually at this point, the tear encircling the edge of the cornea for a variable distance (usually at its upper and inner quadrant) according to the force and direction of the injury On healing, a staphyloma may form at this point

[illegible]

familial type of disease in which successive generations contain members who have fragile bones, among other members who are healthy; the latter have white scleras Those who have fragile bones have scleras which are definitely blue in color.

form within 24 hours. After 36 to 48 hours these adhesions become so dense that it is often impossible to break them except by operation. The dilated, often irregular and rigid pupil is one of the most characteristic objective symptoms in acute congestive glaucoma.

In a severe attack of acute inflammatory glaucoma the vision is severely reduced, often to light perception. No part of the fundus can be seen with the ophthalmoscope. If the condition progresses, the increased tension of the eyeball causes an extravasation into the optic nerve disk which results in blindness

Often the ophthalmologist discovers a simple glaucoma, the diagnosis of which is made by observing the acuity of vision, charting the visual field, making repeated estimations of the tension, and interpreting the findings presented when the ophthalmoscope and the slit lamp have been employed in the examination. Simple glaucoma is often difficult to discover because tension of the eyeball is not always present at the time of the examination, the tonometer may reveal a rise in tension only after repeated tests on different days. Progression of the disease destroys vision.

The patient complains of dimness of vision with the appearance of concentric rings of color surrounding the source of bright light; for instance, a street light.

TUMORS OF THE EYEBALL

The irides may contain dark brown spots (melanomas), due to congenital aggregations of retinal pigment epithelium As a rule, these are benign but occasionally they take on malignant proliferation Any increase of size of such spots in middle-aged persons causes anxiety to the ophthalmologist

True intra-ocular tumors are rare When they are present, they are of two varieties; namely, retinoblastomas or gliomas of the retina, and sarcomas of the choroid The sarcomas of the choroid are frequently referred to as malignant melanomas.

Retinoblastoma. The retinoblastoma, commonly known as glioma of the retina, probably always congenital, occurs in children less than 5 years old, usually in one eye, but often in both, occasionally in successive children of the same family. The attention of the parents is attracted by the yellow reflex, easily seen through the pupil, which is usually dilated

The ophthalmoscope shows small whitish or yellowish plaques (calcium deposits) with metallic luster, either covered by detached retina or growing into the vitreous, the surface often presenting newly formed blood vessels and sometimes hemorrhages

In the glaucomatous stage there are pain, increase of tension and other symptoms of glaucoma. The tumor increases in size and extends into the vitreous. Very soon the growth can no longer be seen on account of turbidity of the media.

As the tumor increases in size, there are enlargement of the globe and exophthalmos, and then perforation takes place The growth passes backward along the optic nerve to the brain, and forward through the cornea and sclera, increasing in size rapidly, involving all tissues with which it comes in contact and forming a large vascular and ulcerating mass. Metastasis occurs to the neighboring lymph nodes and to the cranial bones, and becomes widespread, causing death

Sarcoma. Sarcoma of the eye arises in the iris, choroid and retina. Sarcoma of the *iris* grows rapidly, extends to the corneosclera, perforates the globe and gives rise to metastasis. Sarcoma of the *choroid* arises from malignant proliferation of the stroma cells of the outer layers. It forms at first a mass, raising the retina over it. By the process of growth, increased tension is produced, and rupture occurs in the subretinal space. The *retina* remains in contact with the tumor at the summit of the head, but is detached from the choroid at the sides. As the tumor progresses, the retina is more and more detached, until no part remains in situ The lens then becomes opaque. The tumor may fill the globe before perforating the sclera, or

Diseases of the Iris and Ciliary Body. The iris, the ciliary body and the choroid form the second coat of the eyeball. The iris is in front, the ciliary body is contained in the folds of the choroid, which forms with the lens the partition between the anterior and posterior chambers of the eye. *All these structures contain blood vessels and thus* are the source of the nourishment for the eye. These structures together comprise the uvea or uveal tract Disease affecting one of these structures is likely to involve all of them and may be termed uveitis.

The *iris* is a circular membrane with a circular opening, the pupil, which serves to [illegible] the lens to the interior of the eye. The iris [illegible] the pupil is contracted and it hangs free of [illegible]nt of disease conditions of the uvea, advantage is taken of these responses of the iris

The color of the iris depends on pigmented cells of its stroma and on the cells of the retinal pigmented layers The muscles of the iris are the sphincter pupillae (third cranial nerve) and the dilator pupillae (sympathetic innervation).

The *ciliary body* is contained within that portion of the tunica vasculosa stretching from the anterior part of the iris to join the choroid It is composed of the ciliary muscle and the ciliary processes, blood vessels and nerves.

The blood supply is derived from the greater circle of the iris and the anterior ciliary arteries. Some of the veins pass posteriorly to join those of the choroid, while others from the ciliary muscles pierce the sclera and course beneath the conjunctiva.

The ciliary processes are meridianally arranged vascular folds forming a circle These vascular folds supply nutrient fluids to the interior of the eye, especially the cornea and lens. The ciliary muscle is the muscle of accommodation. When it contracts, it draws the ciliary processes and choroid forward and inward, thus allowing the suspensory ligament to relax and the lens to become more convex. The ciliary body contains within its substance a nerve plexus with ganglion cells.

The congenital malformations of the iris include pupillary membranous changes. Normally the membranous covering of the pupil is absorbed, but part may persist. Of the congenital malformations of the iris the common one is *coloboma*, a notching in the inferior half of the iris, and often associated with coloboma of the choroid

Occasionally the two irides will be of different colors, or a part of an iris may have a different color from the rest This condition is known as *heterochromia*. It may be due to iritis but more frequently it is congenital

Loss of Power of Accommodation. In paralysis of the ciliary muscle distant objects can be clearly seen but near objects are indistinct This condition must not be confused with (1) reflex iridoplegia (loss of the pupillary light reflex) or (2) accommodative iridoplegia (loss of the pupillary contraction for near vision). Reflex iridoplegia and accommodative iridoplegia both depend on the integrity of the same portion of the oculomotor nucleus Cycloplegia is one of the symptoms of complete third nerve paralysis, is a common symptom in diphtheritic paralysis, and may be present in multiple sclerosis

Iritis, Iridocyclitis and Uveitis. In consequence of its vascularity the iris is a frequent site of inflammation When inflamed, it may adhere to the lens behind, forming a posterior synechia An anterior synechia is an adhesion in which, on account of a perforation of the cornea, the iris washes forward and becomes attached to the cornea in front

Inflammation of the iris is so frequently associated with inflammation of the ciliary body that in most cases these two conditions can be distinguished *only by an* experienced ophthalmologist *Consequently, here this condition will be described* as *iridocyclitis*, which means an inflammation that involves the iris, the ciliary body and often the choroid.

The causes of iritis and often iridocyclitis, if the involvement is more pronounced and accompanied by a more intense pericorneal injection, tenderness *in the ciliary* region, swelling of the upper lids, turbidity of the aqueous, and increased tension.

Diseases of the Sclera. Diseases of the sclera are not common. The most frequent disease of the sclera is inflammation, which may be either superficial or deep. The superficial inflammations of the sclera are generally of the lymphatic part. Scleritis, however, an inflammation of the sclera involving the entire thickness, is a serious condition characterized by severe pain, frequently extending to the neighboring parts of the eye and to the forehead. In this condition the tension of the eyeball often becomes increased and a secondary glaucoma ensues. On examination there are discernible well-marked violet patches or dark red patches adjacent to the cornea. If uveitis, as is often the case, accompanies the scleritis, vision is often interfered with and may sometimes be lost entirely. Thinning and bulging of the sclera are known as staphyloma of the sclera

Diseases of the Choroid. The choroid or vascular coat of the eyeball extends forward and is folded at the separation of the anterior chamber of the eye from the posterior chamber

Coloboma. Coloboma of the choroid is a congenital defect of the choroid and retina which is manifested by a large white patch bordered with pigment, usually situated below the disk. The white patch is the exposed sclera. Retinal vessels pass across this area. There is a scotoma (or scotomas if the condition is bilateral) corresponding to the defect or defects.

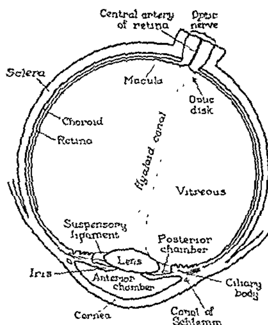


Fig. 4-5 Coats of the eyeball and associated structures

Inflammation. Inflammation of the choroid, or choroiditis, may be suppurative or exudative. Suppurative choroiditis occurs when the choroid with other ocular structures is involved in a purulent inflammation, usually extending from the orbit

The common form of choroiditis described by the ophthalmologist is the exudative form and properly termed *chorioretinitis.* It may be caused by syphilis or tuberculosis, but usually no cause can be assigned. This condition does not present any external symptoms or signs. The patient complains of disturbances of sight, diminution in vision due to opacities in the vitreous, distortion of objects, and a reduction or loss of vision in that part of the field which corresponds to the area of exudation. Very often the patient complains of seeing a black spot, which is the manifestation of a positive scotoma. There are often flashes of light, sparks or bright circles before the eyes

If an area of the retina which is concerned with peripheral vision is involved, the defect of vision may not be noticed, but if the macula is involved, the complaint will be a marked reduction or loss of central vision

On ophthalmoscopic examination the vitreous often is hazy, and patches of exudation varying in size, shape and position are reported by the ophthalmologist. The areas of exudation are colorless with ill-defined margins. There is elevation of the retinal vessels which pass over these areas. In mild instances the exudation may become absorbed. More commonly, however, the exudate becomes organized and, owing to thinning of the areas of exudation, the whitish sclera shows through. Through these thinned atrophic areas choroid vessels surrounded by black pigment, especially at the margins, are reported

responding half of the optic nerve. When the nerve reaches the optic chiasm, it splits into two parts, one (internal fibers) going to the opposite side of the brain, and the other (external fibers) to the ganglia on the same side of the brain. Posterior to the chiasm the nerve fibers form the optic tracts The optic tracts, after leaving the chiasm, wind around the crura cerebri to the external geniculate bodies; thence they pass to the thalami and anterior corpora quadrigemina and are continued backward into the cuneus lobule of the occipital lobe of the brain.

The retina is an extension of the optic nerve dispersed over the whole inner part of the lining coat of the eyeball Where the optic nerve begins, this dispersion is termed the disk. In the visual fields there is a blind spot corresponding to the disk. Away from the disk are the macula lutea and fovea centralis or region of most distinct vision.

Hereditary Degeneration. In pigmentary degeneration of the retina morbid heredity is definite. The characteristic may be dominant, recessive or sex-linked recessive. The disease occurs from soon after birth, to and through middle life

The ophthalmologist describes first a narrowing of the field of vision and twilight and night blindness. The optic nerve head is usually pale There are deposits of dark pigment, irregular in size and shape, connected by fine pigmented lines. The *pigmentation is midway between the extreme periphery of the retina and the region* of the macula, and is bilaterally symmetric. The macular region is the last part of the retina to be involved. The disturbances of vision correspond to the retinal lesions. The retinal vessels are reduced in size. The retina is atrophic and choroidal vessels are exposed. The progress of the disease is slow, and there are no remissions

Congenital deaf-mutism, polydactylism, defect of genital development, mental defect, convulsions, epilepsy and obesity like that seen in Frolich's syndrome are often associated with pigmentary degeneration (see Chapter 15).

The diagnosis is usually made with ease by an experienced ophthalmologist.

Acquired Degeneration. The retina may undergo a chronic progressive degeneration consisting of atrophy of the retina with characteristic deposits of pigment. Along with or as a part of general retinitis there may be a *macular degeneration*. The condition is bilateral, the maculae are the seat of pigmentary changes, and central vision is reduced This commonly occurs in elderly people.

Obstruction of the central vessels of the retinas causes immediate blindness If the artery is obstructed, the retina is pale with a cherry red spot at the fovea. If the vein is obstructed, there are congestion and enlarged tortuous veins present everywhere in the fundus.

Retinitis. Inflammation of the retina is rarely limited to the retina alone, but usually is associated with disease of the choroid and is thus termed chorioretinitis. Inflammation of the retina may be associated with inflammation of an optic nerve, and if so, is known as neuroretinitis

As retinal disease is usually secondary to some extraocular cause, it is in the majority of cases a bilateral affection The varieties and diagnostic significance will be indicated in various parts of this text A partial listing is as follows:

Neuroretinitis of hypertension occurs in cases of arterial hypertension (see Hypertension, Chapter 10). The papillitis may be so marked that it is difficult to determine whether it is of vascular or of intracranial origin. In neuroretinitis the retinal vessels are altered and seem interrupted where they are covered by the swelling. The arteries are thin; the veins are tortuous and distended. There are flame-shaped hemorrhages and the so-called cotton-wool exudates. *Neuroretinitis of glomerulonephritis* is distinguishable from that occurring in hypertension (see Diseases of the Kidneys, Chapter 11). In *congenital syphilis* retinitis pigmentosa may occur. In acquired syphilis both retina and choroid are likely to be affected and the chorioretinitis is regarded as a secondary symptom. About 1 of every 4 who have leukemia has retinitis (*leukemia neuroretinitis*). *Diabetic retinitis* seems to be characteristic (see Diabetes Mellitus, Chapter 14).

The symptoms of affections of the retinas are marked disturbances of vision or

are the same. The distinction in the terms is based rather more on degree of involvement than on the anatomic structures involved.

Both iritis and iridocyclitis have often been attributed to *chronic focal infection.* However, there are but a few patients who have the disease in whom focal infections can be demonstrated Abnormal intestinal flora and intestinal toxins cannot be demonstrated. Iridocyclitis may be a part of: (1) Syphilitic iritis or iridocyclitis which occurs during the secondary stage of syphilis; (2) Gonorrheal iritis or iridocyclitis which occurs in a few of those who have gonorrheal urethritis; (3) Tuberculous iritis or iridocyclitis which occasionally occurs; (4) Iritis or iridocyclitis which may be mentioned as a complication of diabetes, gout and rheumatism.

Despite the fact that all are agreed that usually an iritis or an iridocyclitis is of systemic origin, general examinations often do not disclose a definite cause.

The chronic or relapsing form of iridocyclitis, which often affects younger persons, frequently is termed uveitis.

The symptoms of iridocyclitis consist of pain, photophobia, lacrimation and interference with vision. The pain is often severe and may be referred to the region of the eyeball, or it may extend to the forehead or temple; it is worse at night than by day. Often there is tenderness of the eyeball On examination the iris appears swol-

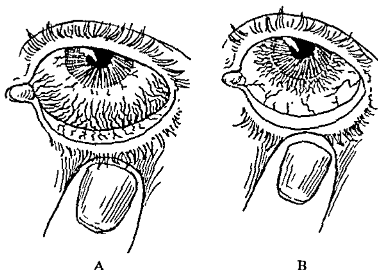


Fig 4-6. Distribution of dilated blood vessels in conjunctivitis and in iridocyclitis A, conjunctivitis B, iridocyclitis

len and dull, it has lost its color and is now greenish blue or gray and may be of a smoky appearance The pupil is contracted, irregular and sluggish in action One of the most characteristic of the external appearances of this condition is a marked circumcorneal injection and more or less conjunctival injection. It is important that iridocyclitis be differentiated from an acute catarrhal conjunctivitis, because in iridocyclitis the instillation of atropine is most important in treatment (Fig 4-6). Likewise the condition should be differentiated from glaucoma because the instillation of atropine in a glaucomatous eye is disastrous It should be remembered that generally in iritis the pupil is small, gray and sluggish and irregular in outline after the use of atropine In glaucoma the pupil is dilated, oval and immovable The cor- [illegible] cornea in glaucoma is insensitive In acute iritis the [illegible] whereas in glaucoma the conjunctiva is congested [illegible] ill tension is usually normal; in glaucoma, it is increased.

Diseases of the Retina. On the interior of the eye the expansion of the optic nerve forms the retina. The retina is divided into two lateral halves, each supplied by a cor-

Pathologic Conditions. There are three varieties of paralysis of the iris, or iridoplegia, with pupils small or of medium size, as follows: (1) loss of response to *light*—reflex iridoplegia; (2) loss of response to *accommodation*—accommodative iridoplegia; (3) loss of response to *irritation of the skin of the neck*—absent skin reflex

Common Abnormalities of Iris and Pupil. The common abnormalities of the iris and pupil, together with their possible diagnostic indications, may be stated as follows:

Iris and Pupillary Outline. Inflammation of the iris is often of idiopathic origin If iritis is present, the iris, if normally blue or gray, becomes darker, the pupil responds sluggishly to the light and, if the disease is unilateral, is smaller than the other pupil because of the iritic congestion and consequent swelling. There is a narrow zone of pinkish hyperemia around the edge of the cornea. If the iris is brown or black, little change of color occurs. While one iris may normally differ in color from the other, if one is green and the other blue the existence of iritis should be strongly suspected In many cases iritis is unilateral and is prone to relapse. Syphilitic iritis occurs only during the secondary stage of the disease, is commonly bilateral, and rarely relapses.

An irregular outline of the pupil is due to iritis and subsequent adhesions between the posterior surface of the iris and the anterior surface of the lens, posterior synechia.

Anisocoria. Inequality of the pupils may be present in healthy persons and in those whose eyes refract unequally.

Adie's Syndrome. Adie's syndrome is an anomaly in which there is one myotonic pupil, often associated with absent tendon reflexes. The condition is generally unilateral and the defective pupil is larger than its fellow The cause is unknown except in instances where it is associated with the Pancoast syndrome

Hippus. A rapid contraction and dilatation of the pupil on sudden exposure to light is normal in some healthy persons It is also seen in the early stage of acute meningitis, in disseminated sclerosis and in hysteria In Cheyne-Stokes respiration the pupils may be dilated during the period of rapid breathing and contracted in the apneic interval

Argyll Robertson Pupil. If the pupil does not respond to light and shade, but does respond to accommodation, it is of the type called the Argyll Robertson pupil. The condition most frequently is present as a symptom of locomotor ataxia and perhaps is due to changes in the third nerve nucleus which presides over the light reflex, the portion which regulates the accommodative contraction not being involved The loss of the light reflex may also be due to degeneration of the ciliary ganglion The pupil in this condition is usually contracted because the lesions in the cervical segment of the spinal cord interfere with the dilating mechanism Late in the disease the accommodation reflex also may be lost A similar pupillary condition is seen as a symptom of intracranial syphilis and progressive paresis of the insane

Accommodative Iridoplegia With Preserved Light Reflex. This condition is the opposite of the Argyll Robertson pupil It is of infrequent occurrence and may denote a lesion affecting a portion of the oculomotor nucleus in which lie the cells causing accommodative reaction It may also, but not always, exist with the cycloplegia which occurs after diphtheria

Unilateral Dilatation. One pupil may be dilated as the result of disease of the optic nerve, as in optic atrophy, or there may be lessened transparency of the media, as in cataract and glaucoma If the pupil of the diseased eye does not react directly to light, but does react when the light is thrown into the sound eye (consensual or indirect reaction), it shows that the disease is in the optic nerve or tract and that the oculomotor nerve of the diseased side, its nucleus, and nuclear connections with

complete blindness. In the beginning, the field of vision is usually contracted peripherally for colors and there may be reversal of the color field. The blind spot is enlarged and hemianopsia or scotomas may be present.

Examination for disorders of the retinas is performed by means of the ophthalmoscope and direct retinoscopy Retinitis is almost always bilateral and does not present external signs or symptoms. Examination reveals an indistinctness of retinal details, congestion of the disk with blurring of its edges. A retinitis is characterized by circumscribed exudations appearing as soft, white spots or patches of variable size which may be discrete or confluent. The spots occur principally along the retinal vessels and in the macular region. Often there are tortuosity and distention of the retinal veins, which appear to be darker than they are when normal The vessels may be obscured in part by swelling and exudation Hemorrhages are present and are often described as rounded, soft, or flame-shaped. In retinitis accompanied by choroiditis, opacities in the vitreous may be seen

Retinal Hemorrhage. The vascular changes accompanying arterial hypertension are the commonest cause of retinal hemorrhages as described in the section on hypertension. Chronic nephritis may be the causative condition and so also may the hemorrhagic blood states, as in scurvy, hemophilia, purpura and the grave anemias Retinal extravasations may also be significant of malarial fever, septicemia, pyemia and leukemia, although in the last a retinitis is commoner than retinal hemorrhage

Detachment of Retina. The retina may become detached. When it is detached, there is a loss of vision in the visual field of this part of the retina A small loss of vision from a detachment of the retina may not be noticed by the patient. However, if there is an extensive detachment of the retina, the patient observes a visual disturbance which may be described as a cloud or curtain hung before the eye Early *symptoms are metamorphopsia*, and flashes of light, or photopsia. Detachments of the retina are easily visualized by means of the ophthalmoscope They are commoner in myopic eyes than in other types of eye

THE PUPIL

The pupil is the aperture in the iris which controls the amount of light reaching the lens and consequently the interior of the eye The points to be observed about the pupil are its state of dilatation or contraction, inequality (anisocoria), response to light, response to accommodation, and the skin reflex

The responsiveness of the pupil to light is determined for each eye separately by the use of an artificial light or by asking the patient to look at the light from a window With the patient still keeping the eyes in the same direction, the hands of the physician are placed over and close to, but not touching, the eyes One hand is then suddenly removed, and the behavior of the pupil is noted Normally the pupil contracts on exposure to light—the *direct reflex* In normal eyes the pupil of the covered eye will also contract—the *indirect reflex* Particular care in this examination is desirable. Artificial light in a dark room should be employed In the modern lighted room the light reflex cannot be determined with the lights on Turn the lights off before attempting to test for the light reflex with an artificial light. While the patient, with one eye covered, looks toward the darkest part of the room, the light is brought suddenly before the uncovered eye, at a distance of 3 or 4 feet (about 91 or 122 cm.) so that the pupillary accommodation reflex may be eliminated.

Response to Accommodation. Since the pupil grows smaller when the eyes converge and the ciliary muscle contracts in the act of accommodation for near objects, this function should also be examined. Let the examiner place his finger tip 12 or 15 inches (30 or 38 cm) from the eye, nearly in line with some distant object, and direct the patient to look first at the finger and then at the distant object until it is decided whether or not the pupil contracts when the patient is looking at the finger.

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the corpora quadrigemina, and through the latter with the opposite optic tract, are not involved. Unilateral dilatation may be due to irritation of the cervical sympathetic by a tumor of the neck, by aneurysm of the aorta, and when limited to the right eye, by an aneurysm of the innominate artery. One pupil is dilated in unilateral paralysis of a third nerve.

Bilateral Dilatation. Double atrophy, amaurosis or blindness from any cause will obviously give rise to dilatation and failure of the light reflex. Mydriasis may result from syncope, shock, nausea and aortic regurgitation. The pupils may be dilated in neurasthenia, hysteria and strong emotion; in severe dyspnea and asphyxia; in cerebral hemorrhage, thrombosis, tumor and abscess; in the later stages of meningitis and diphtheritic paralysis, from lesions of the oculomotor nerve or nucleus; in coma following an epileptic convulsion, and after administration of drugs. Some of the drugs which have a mydriatic action, local or constitutional, are alcohol, atropine, chloral, chloroform, cocaine, hyoscyamus, nitrous oxide, strychnine and tobacco

When both pupils are dilated, the eye has a peculiarly brilliant expression, which may be particularly noticeable in mania, in fevers attended with active delirium, in exophthalmic goiter, and in poisoning with belladonna.

Contracted Pupils. Contraction of the pupils (miosis) may be due to irritation of the oculomotor system, to paralysis of the dilators or to the administration of drugs

The pressure of a mediastinal tumor, if sufficiently great to paralyze the sympathetic (dilator) fibers in the upper part of the thorax, may explain unilateral miosis. Unilateral cerebral lesions, so placed and of such a character as to irritate the oculomotor center, may cause unsymmetric miosis

A certain degree of miosis and sluggish contraction of the pupil is normal in old age. The pupils are contracted during sleep in a healthy person

Congestion of the iris, such as occurs in the injected eyes in rickettsial fevers, causes miosis; so also with mitral insufficiency and other conditions producing venous congestion The pupils are contracted in retinitis and when photophobia exists

Bilateral disease of the cervical segments of the spinal cord and spinal column, by paralyzing the sympathetic dilator fibers, may allow miosis Symmetric miosis may thus be significant of locomotor ataxia in particular, disseminated sclerosis, general paresis, spinal meningitis, tumor or hemorrhage of the cord, bulbar paralysis, hemorrhage into the pons, and tuberculous disease of the cervical vertebrae. Irritating lesions of the brain—notably cerebral meningitis, cerebral or dural hemorrhage and tumor or abscess of the brain—by stimulating the third nerve center, will cause miosis. Miosis is present in the early stage of sunstroke and may also be present in the uremic state

Certain drugs have a characteristic action in contracting the pupil, particularly opium and its alkaloids. Others are eserine and pilocarpine

Absent Skin Reflex. If the pupil does not dilate when the skin of the neck is pinched or pricked, it may be due to the atrophy of the iris in a glaucomatous eye or to posterior synechia following iritis It is not infrequent in general paresis.

DISEASES OF THE LENS

The alteration of the refractive power of the lens is accomplished by changes in diameter and in shape of its anterior surface according to the distance between the [illegible]

lens invariably result in loss of transparency in the parts affected This condition of partial or complete loss of transparency is called cataract.

Cataract. The earliest stage in the development of cataract is an accumulation of fluid either as droplets beneath the capsule or in spindle-shaped spaces between the lens fibers. Clinically this stage can be recognized by inequalities in the refractive indices of the fibers and fluid which give rise to light and dark streaks when light is thrown into the eye by the mirror.

The essential and common factor in the production of cataract is the coagulation of the proteins of the lens which accompanies advancing years However, many different factors, such as radiant heat, luminous and ultraviolet rays, and radium, may cause cataracts. Ultraviolet rays alter the permeability of the lens capsule. Dinitrophenol, used for reducing body weight, may produce posterior cortical cataract The occurrence of cataract in tetany due to parathyroid deficiency suggests a definite association with the role of calcium metabolism Cataract also occurs in association with myotonia atrophica and ergotism

Cataracts are classified according to the situation and the extent of the opacity or opacities in the lens and according to the age of the patient.

Cataracts of Congenital Origin. The commonest forms of congenital cataracts are lamellar and anterior capsular; less common are the central or total.

Lamellar cataract occurs early in infancy. The opacity in lamellar cataract is situated in the layers surrounding the center of the lens, which itself usually contains punctate opacities; the superficial cortex is clear. Lamellar cataract is due to a period of malnutrition at some stage of late intra-uterine or early infantile life. Epithelial structures are most affected, and characteristically epithelium persists where ordinarily it is cast off. Epithelium persists in the lens and in the enamel of the teeth. Lamellar cataract is almost invariably accompanied by defective enamel in certain of the permanent teeth. The hypoplasia differs essentially from the condition of the teeth in congenital syphilis It is often due to maternal rubella.

Cataracts may result from premature birth

Anterior and posterior cataracts are of congenital or acquired origin. Anterior cataracts are designated anterior capsular and anterior cortical The posterior cataracts are posterior opacities called posterior polar and posterior cortical cataracts.

The child is brought for examination on account of defective vision Objects are held very close to the eyes

Senile Cataract. A senile cataract rarely occurs in persons less than 50 years of age Cataract occurs equally in men and women. It is usually bilateral, but develops earlier in one eye than the other. Cases of hereditary predisposition have been recorded, and in some of these the cataract develops at an earlier age in successive generations.

The appearance of black spots in front of the eyes is usually the first symptom. The spots differ from the ordinary muscae volitantes occasionally complained of in normal eyes, and much exaggerated in cyclitis, in that they are stationary, retaining their relative position in the field of vision in different positions of the eye. There may be doubling or tripling or even more duplication of the objects seen. This is often worse on looking at bright lights Eventually the central area becomes affected and vision steadily diminishes until only perception of light remains.

The pupil in old people is seldom so black as in the young, and is sometimes distinctly gray. If the grayness is uniform, cataract is not diagnosed unless definite opacity is shown on examination with the ophthalmoscope. This grayness without opacity is caused by increase in the refractive index of the cortex of the lens in old people, and is due to increase of reflection and scattering of light

The nucleus in the common senile cataract undergoes little change and does not become opaque, but eventually the whole of the cortex is cataractous. The cataract is then said to be ripe or *mature* At this stage it will be found that the anterior chamber has regained its normal depth. The watery fluid has been absorbed from the lens, which has again returned to its normal volume. *This is an important guide* to the most favorable time for operation

In *incipient* senile cataract radial spokes or sectors of opacity are seen, with clear areas between them. They are difficult to see in daylight or by oblique illumination, and cataract cannot be diagnosed without confirmation with the ophthalmoscope With the pupil undilated, only the ends of the spokes are seen, but when the pupil is dilated, the linear opacities are often found to be the apices of sectors, with their bases toward the periphery. They generally begin in the lower part of the lens, especially the lower nasal quadrant.

Secondary Cataract. A form of secondary cataract is the opacity which persists or follows after the extraction of the lens.

Cataract in diabetic persons is by no means always diabetic in the proper sense of the term Senile cataract of the usual type, following the usual course, often occurs in elderly diabetic patients. Cataract in young diabetic patients is a secondary or complicated cataract and termed *diabetic cataract.*

Owing to exposure to roentgen rays or radium, cataracts may form *Irradiation cataract* resembles the early posterior cortical stage of *glassworkers' cataract* One course of deep roentgen rays may suffice There is a considerable latent period, which may be at least two years Only the gamma rays of radium seem to be nocuous.

THE VITREOUS BODY

Opacities. Black specks, floating before the eyes, may be seen by normal persons These specks (muscae volitantes) are opacities of various kinds which cast shadows on the retina, thus appearing as dark spots in the field of vision The corpuscles circulating in the retinal blood vessels at times may be seen as golden-colored specks Other muscae may be due to small specks in the vitreous Some types of muscae cannot be seen with aid of the ophthalmoscope.

Under abnormal conditions muscae may be of sufficient numbers to interfere with vision and to become visible by the ophthalmoscope They then indicate some disease of the uveal tract, particularly of the ciliary body; they are found in cyclitis and choroiditis In the more severe instances muscae may resemble flakes and threads. Such large opacities are often present after hemorrhage into the vitreous.

Fluid Vitreous and Specks Before the Eyes. Fluid vitreous is common in cases in which opacities are present, and is associated with the same causes The degeneration of the vitreous which leads to fluidity often causes the deposition of crystals of cholesterol, which sink to the bottom of the vitreous chamber, but are stirred up by movements of the eye. They then appear as a shower of specks of a bright yellow color (synchysis scintillans).

Blood. Hemorrhage into the vitreous may result from arteriosclerosis or inflammation of the retina, from contusions or wounds of the eye or may appear without apparent cause Hemorrhages, filling the vitreous with blood, are suspected when no reflex can be obtained on throwing in light with the mirror It may then be possible to see a red mass behind the lens by oblique illumination

Severe vitreous hemorrhage may occur in apparently healthy young adults *It* has a great tendency to attack both eyes in succession and to recur, so that though absorption may be complete in the early attacks, permanent defect or complete loss of sight, retinitis proliferans, or dense vitreous opacities may ultimately follow from damage to the retina It is characteristic of vitreous hemorrhage that absorption usually takes place without organization, owing to the absence of fibroblasts in the vitreous. When organization occurs, as in so-called retinitis proliferans, it is most marked near the disk, from which membranes and strands stretch forward. Even [illegible] the absence of some general disease.

[illegible] is present in the vitreous in *cases of plastic* [illegible] membranes stretching across behind the lens. In [illegible] in syphilitic and possibly tuberculous subjects, minute bunches of newly formed blood vessels project from the disk or retina.

Parasites. Cysticercus, when present, may be seen ophthalmoscopically as a pearly translucent mass with peristaltic movements

THE OPTIC NERVE

As the optic nerve enters the eye, it is contracted and forms the disk or papilla It is readily seen with the ophthalmoscope as a round spot somewhat lighter in color than the surrounding eyeground. Coming from a depression or cup in the disk, called the porus opticus, are the retinal arteries and veins. A certain amount of cupping is normal, but if wide and deep, with overhanging edges over which the vessels can be seen to dip, it is indicative of glaucoma.

Sometimes, as in brain tumor and in malignant hypertension, the papilla, disk or optic nerve head is swollen. When this condition occurs, it is called choked disk or papilledema.

Inflammations of the optic nerve, known as optic neuritis, consist of two groups of affections, one arising within the eyeball (papillitis) and the other arising behind the eyeball (retrobulbar neuritis).

Papilledema or Choked Disk. Papilledema or choked disk is a noninflammatory swelling of the optic nerve head which often results from increased intracranial pressure, from malignant hypertension, or from obstruction of the orbital veins. The condition is usually bilateral, though there may be different degrees of swelling in the two eyes. In rare instances only one eye is affected

On ophthalmoscopic examination of the fundus in instances of intracranial hypertension there are swelling and protrusion of the disks, distortion and tortuosity of the retinal veins, and hemorrhages on or near the swollen papilla. There usually is a sharp limitation of the condition to the optic nerve and to the retina immediately adjacent to the nerve head The degree of projection of the disk is determined by the difference in refraction between its most protruding part and the adjacent but unaffected retina This difference is expressed in diopters. The disk is not considered to be choked unless there is a refractive difference of 2 diopters or more. In the early stages of a choked disk the blind spot is enlarged As the intracranial pressure increases, the vision may become gradually less until finally blindness ensues. However, immediate relief of intracranial pressure prior to blindness often restores vision Choked disk may occur as the result of a number of intracranial conditions such as hydrocephalus, brain abscess and suppurative meningitis. It is important to keep in mind that choked disk accompanied with neuroretinitis is characteristic of malignant hypertension.

Choked disk does not accompany growths in the pituitary body. It occurs late, if at all, in lesions of the motor cortex, and is most frequent in neoplasms of the cerebellar parieto-occipital regions and midbrain. The condition is symptomatic of tuberculous, nontuberculous and suppurative forms of the meningitis.

Retrobulbar Neuritis. Inflammations of the optic nerve behind the eye are termed retrobulbar neuritis There is slight or no change in the appearance of the disk unless a tumor of the brain is present

The common cause of retrobulbar optic neuritis is syphilis. In rare instances optic neuritis may be caused by encephalitis, meningitis, acute febrile diseases, or by poisoning, especially lead. Retrobulbar optic neuritis may develop in young adults in association with disseminated sclerosis, without other symptoms. Diphtheria and diabetes may cause this disorder of the optic nerve. Unilateral optic neuritis occurs only when there is disease of the bones of the orbit or inflammation of the orbital tissues. It often exists without an assignable cause

The first symptom is unilateral or bilateral blurring of vision with pain in and above the affected eye brought on by ocular movements. The reduction of vision is rapid, reading is impossible within 2 or 3 days after the onset. One eye may be affected first, but the condition is bilateral

The pupils are equal and circular and react equally to light. They are sluggish Central vision is reduced or abolished. The visual field, except for the central scotoma, is normal. The optic disk at first is congested and shows haziness of the margins Temporal pallor then appears which bears no relation to the disturbances of vision Usually within a few weeks vision begins to improve Rarely is vision lost in the first attack There is a strong tendency for the trouble to recur.

Retrobulbar neuritis without edema of the disks is distinguished from that due to various poisons, such as lead, arsenic, thallium and methyl alcohol, as indicated by the history and appropriate examinations.

Neurosyphilis is not of etiologic importance Tumors of the hypophysis pressing on the intracranial portion of the optic nerve can be excluded on the basis of roentgenograms of the sella turcica

The prognosis of retrobulbar neuritis is at best doubtful, for complete recovery or for complete blindness Disseminated sclerosis may appear immediately or after many years When disseminated sclerosis develops in other parts of the nervous system, the process is acute and severe

Toxic Amblyopia. There are a number of causes for toxic amblyopia, among which quinine, methyl alcohol, overuse of tobacco, vitamin deficiency and uremia may be mentioned

The toxic amblyopias are manifested by a gradual diminution in acuteness of sight. The dimness of vision may be more definite in bright light than in dim light There are central color scotomata The ophthalmoscopic signs are usually minimal, but pallor of the temporal side of the disk, color scotoma, may occur as the condition progresses.

Atrophy of the Optic Nerve. Inflammation of the optic nerve, with congestion, hemorrhage and exudation into its substance, may affect the nerve posterior to the globe, *retrobulbar neuritis,* the nerve at its end, *papillitis,* the retina, *retinitis* In course of time there may be connective tissue proliferation and consequent atrophy of the nerve fibers, giving rise to secondary *optic atrophy*

Atrophy of the optic nerve occurs also as simple atrophy or primary atrophy, which is a noninflammatory condition. The cause is unknown There may be secondary atrophy of the optic nerve which is postneuritic, secondary inflammatory atrophy, or atrophy of nutritional origin

Primary Atrophy. In primary or simple optic atrophy there is degeneration of the nerve fibers The common causes of simple atrophy are cerebrospinal diseases, especially tabes dorsalis during its inception. Simple atrophy is less frequent in general paralysis of the insane It may occur in multiple sclerosis. When it does occur as a part of multiple sclerosis, it follows retrobulbar neuritis; it rarely results in complete blindness though often there is a transient blindness Simple optic atrophy may accompany systemic syphilis, malaria, diabetes, acromegalia, oxycephaly, profound hemorrhage with loss of consciousness (anoxia), the specific fevers, arteriosclerosis and certain poisonings, including methyl alcohol, lead and arsenic poisoning. It results from a *thrombosis of the central retinal arteries,* and it may occur in connection with choroiditis, retinitis, glaucoma, aneurysm of the internal carotid artery and orbital inflammation There is a hereditary form of the disease which is commoner in young men than in others.

Secondary Atrophy. Secondary optic atrophy is usually consequent to an optic neuritis, expanding intracranial lesions, and tumors of the optic nerve. Retrobulbar neuritis, syphilitic chorioretinitis, and retinitis pigmentosa may also be responsible for atrophy In some who have chronic hydrocephalus a greatly distended third ventricle may press on the chiasm and produce optic neuritis and atrophy.

Optic Atrophy and Arteritis. An optic atrophy may result from an arteritis as in periarteritis nodosa or in the condition known as temporal arteritis

Syphilitic Optic Atrophy. Bruetsch observed the existence of both the inflammatory and the degenerative phases of syphilitic optic nerve atrophy. He emphasized that the degenerative changes in optic atrophy are preceded by an inflammatory exudative phase. Visual field defects may be caused by the exudative processes in the marginal zone before atrophy of the nerve fibers has taken place, and such defects may improve or disappear after antisyphilitic treatment. Klauder and Meyer have stressed the necessity of an early ophthalmologic and perimetric examination of all patients who have neurosyphilis regardless of whether the serologic reactions of the blood and spinal fluid are positive or negative. The presence of pupillary abnormalities calls for examination of the cerebrospinal fluid in order to exclude optic nerve atrophy. It appears, therefore, that the problem of syphilitic optic nerve atrophy as a cause of blindness is concerned principally with early diagnosis. The ophthalmoscope and perimeter are as essential as the spinal puncture in the diagnosis and management of syphilis and its complication, primary optic nerve atrophy

In optic atrophy from any cause the patient complains of a profound disturbance of vision consisting of, on examination, a contraction of the visual fields, blind spot enlarged, color fields reversed, and scotoma.

INJURIES TO THE EYE FROM CONTUSIONS AND RADIANT ENERGY

There is no part of the eye which may not be injured so seriously by contusion or radiant energy as to diminish vision. In some cases the changes are progressive. In all cases a guarded prognosis should be given when these injuries have been sustained

Contusions. A contusion may vary in severity from a small abrasion of the cornea to rupture of the eyeball

Cornea. Injuries to the cornea incident to sharp objects, manifested by only a slight abrasion revealed by staining with fluorescein, heal immediately. A similar small abrasion of the cornea incurred by a sudden fall or a stroke from a blunt instrument causes severe pain The pain is increased on moving the lids, there is much lacrimation as well as reflex blepharospasm The sequence of events, a fall, slight corneal abrasion, and severe pain, is originated by a pre-existing corneal ulcer or results from injury to the fifth cranial nerve at the time of the fall or from pre-existing disease of the fifth cranial nerve.

In some instances of injury to the fifth cranial nerve the corneal abrasion may heal quickly. However, after days, weeks or even months acute pain and lacrimation commence. These symptoms are more evident on first opening the eyes in the morning than at other times. There is no doubt that in these cases the epithelium is abnormally loosely attached to Bowman's membrane, and is likely to be torn off by the lid on waking Such looseness of epithelium and formation of vesicles are characteristic of lesions of the fifth nerve and it is probable that recurrent erosion is due to this cause.

On examination deep opacity may be found which is due to accumulation of lymph in the interlamellar spaces These opacities are generally transient and clear up

Examination by means of the slit lamp reveals that all contusions of the eyeball are followed by the deposition of uveal pigment on the posterior surface of the cornea. There may be ruptures in Descemet's membrane, owing to its elasticity, but ruptures of the cornea are rare

Sclera. Rupture of the globe is generally due to its being suddenly and violently forced against the orbital walls. It is often due to falls or to the eye being forcefully struck by a projecting object, the force having been applied from the inferolateral direction, where the eyeball is least protected by the orbital margin. The wound is oblique, being farther forward internally than externally. It is situated concentrically with the corneal margin The conjunctiva is usually left intact, but severe injuries

to other parts of the eye are inevitably present. The iris is often prolapsed or torn away (iridodialysis) or retroflexed. The lens may be expelled from the eye or may escape under the conjunctiva, or be forced back into the vitreous. A displaced lens leaves the anterior chamber deep The anterior chamber contains blood and there may be hemorrhage into the vitreous. Detachment of the retina may occur, with or without subretinal or subchoroidal hemorrhage. The eye shrinks and sight is lost.

Iris. Most injuries to the iris caused by contusion are due to direct blows with a sudden inward displacement of the cornea.

Traumatic mydriasis may follow a contusion The pupil is immobile, and remains moderately dilated and paralyzed to accommodation permanently. Radiating lacerations of the iris, sometimes extending to the ciliary margin, may occur. In iridodialysis a black biconvex area is seen at the periphery, and the pupillary edge bulges inward With the ophthalmoscopic mirror a reflex can be obtained through the peripheral gap. Iridodialysis is permanent Apart from other injury, however, it rarely causes serious disability.

Lens. Injuries to the iris may cause rupture of the suspensory ligament. The lens is forced back into the vitreous. With the pupil dilated, the edge of the lens may be seen as a gray convex line by oblique illumination, but more readily as a black line with the ophthalmoscopic mirror The lack of support to the iris is detected by its unsteadiness, revealed on movement of the eye

In partial rupture of the suspensory ligament there is astigmatism which is much increased on movement of the head as the lens is thus tilted. Total dislocation of the lens into the vitreous causes a deterioration of vision

In a lens displaced so much laterally that the edge crosses the pupil, uniocular diplopia is present In subluxation the lens is likely to become opaque, owing to malnutrition The pressure of the edge of the lens on the back of the iris and on the ciliary body often originates a severe iridocyclitis and endangers the other eye by sympathetic ophthalmia Secondary glaucoma is frequent

With or without dislocation of the lens, concussion cataract occasionally follows a contusion In most of these instances the capsule has been ruptured The lens gradually becomes opaque The cataract spreads throughout the cortex until the appearance of a mature cataract is present

Vitreous. Hemorrhage into the vitreous is common after contusion. The vitreous chamber may be filled with blood and the eye is without reflexes On oblique illumination a dull red hue may be seen The blood may become almost completely absorbed, but cloudy opacities remain

Choroid. Rupture of the choroid occurs as the result of severe contusion It has also been caused by a bullet passing through the orbit behind the eye. Immediately after the injury the view is obscured by extravasation of blood When the blood has become absorbed, the rupture appears as a curved white streak over which the retinal vessels pass If the choroid is ruptured near the macula, there is loss of central vision. Ruptures of the choroid in which the macula is not involved cause little impairment of vision.

Retina. Detachment of the retina may be due to contusion However, spontaneous detachment of the retina often occurs

Blows on the eye may change the normal bright red color of the retina to a light gray near the papilla This change in color, which is probably due to edema, disappears after some days, and vision is usually restored to normal In some instances vision may be good at first but then central vision diminishes, and pigmentary deposits develop at the macula Hence prognosis should be guarded in all cases of serious blows on the eye.

Optic Nerve. The optic nerve is frequently injured in fractures of the base of the skull. Injuries by sticks or knives penetrating the orbit are rare. Avulsion of the

optic nerve is extremely rare but occurs as the result of wounds from flying missiles or bullets.

Radiant Energy. Radiant energy may be divided into two types: (1) the electromagnetic radiation and (2) the corpuscular radiation consisting of subatomic particles, the most noteworthy of which are the electrons (variously called beta rays and cathode rays, depending on their source) and the neutrons (Cogan).

The radio and diathermy waves cause no effect on the eyes except in the immediate vicinity of a transmitter. An electric current consisting of beamed movements of electrons may cause ocular injury or other injury through electrolysis or by the production of heat in the tissue.

The long infrared radiation which may give rise to cataracts is largely derived from open furnaces used by professional glass blowers and foundrymen Infrared cataracts occur only after exposure to intense heat for many years The cataracts resulting from infrared radiation are characteristically posterior cortical, forming at first saucer-like opacities belonging to the general group of so-called cataracta complicata.

The short infrared radiation which has been harmful to the eye (retinitis) may be obtained from electric arcs, the sun, and quartz and mining lamps.

The amount in the abiotic range of ultraviolet radiation filtering through the atmosphere from the sun is too slight to be harmful except under extraordinarily clear conditions or at high altitudes.

Keratitis resulting from ultraviolet radiation of the sun occasionally occurs with prolonged exposure at high altitudes or in the presence of large snow fields. The lesion consists predominantly of punctate erosions of the epithelium in the exposed portions of the cornea. The symptoms come on after a latent period of 5 to 12 hours; the patient has no feeling of ill effects from being exposed to harmful radiations at the time of exposure The effects are cumulative during an interval of 24 hours and, unlike the skin reaction, no tolerance is acquired by repeated exposures The patient's symptoms are severe photophobia, pain, epiphora and blepharospasm which are incapacitating at the time but seldom lead to permanent injury of any part of the eye.

The corneal lesion resulting from grenz rays and beta rays is keratitis with severe symptoms consisting of epiphora, foreign-body sensation and photophobia, but the latent period is longer and the duration is longer than is the case with ultraviolet effects Susceptibility of the lens to roentgen rays is said to be an inverse function of age, the most vulnerable being fetuses irradiated in utero

Glaucoma may follow roentgen irradiation of the eye. It arises several weeks after irradiation and usually in association with uveitis

The latent period for the development of cataracts following irradiation is usually from 6 months to 2 years but may be as long as 10 or more years. In general the greater the dose the shorter the latent period

A roentgen-ray cataract begins characteristically as an opacity at the posterior pole of the lens It may remain stationary but is usually progressive Progression is usually indicated by the appearance of vacuoles in the anterior cortex and an anterior subcapsular haze from proliferation of the lens epithelium

Cataracts from gamma rays and neutrons are similar to those produced by roentgen rays as regards latent period and structure, and similarly occur with doses that produce no other clinically evident abnormality

Radio waves are not known to produce any physiologic or pathologic effects on the eye, and the effect of diathermy waves is that of a thermal coagulation when locally applied

The long, or far, infrared rays probably can cause a thermal burn of the retina The susceptibility to retinitis may be influenced by nutritional factors which induce a sensitization to visible radiations so that retinal lesions may result from exposure to sunlight (Cogan)

VISION

The disorders of vision which are of diagnostic importance are hemianopsia, alterations in the color fields, amblyopia, and amaurosis.

Minor Disorders. If objects seen have a yellow tint, it may be due to jaundice or the administration of drugs, particularly of santonin. In exhausted neuropathic women or children overuse of the eyes may cause everything to appear red. The small, beaded, semitransparent threads or dots (muscae volitantes), seen in looking at some clear expanse of light, are, as stated, of small diagnostic importance. They appear to be most abundant in hysteria and functional disorders. Flashes or small luminous points of light before the eyes occur commonly after quick changes in position, coughing or straining, and usually are not of diagnostic import. However, they may constitute the aura of epilepsy or migraine Migraine may be preceded by scotomata resembling a cloud, the edges of which are brilliantly lighted or colored The scintillating scotomata appear as bright dots, whirling figures and as bright lines before the eyes

Failing Vision. The causes of failing vision arise from the cornea, iris, ciliary body and choroid, retina, optic nerve, lens and vitreous, and from disuse. The following paragraphs contain a summary of the views expressed by Post in regard to failing vision

Among the corneal causes of visual failure, tuberculosis is common. It is usually considered an allergic manifestation. Corneal degeneration is frequent in old persons. The central areas, anteroposteriorly, may become less transparent. Nodules appear in the posterior elastic membrane that look like small drops of water on the rear surface of the cornea when seen with the corneal microscope. Epithelial degeneration occurs

Corneal ulcers are an important cause of visual failure. They occur throughout life, their causes varying from gonorrhea in infancy through phlyctenular keratitis in youth to malnutrition and the physiologic changes incident to age. In preadolescence the interstitial keratitis of syphilis may cause blindness.

Allergic diseases of the iris, ciliary body and choroid are as frequent in ophthalmologic practice as allergic diseases of other structures are in every other department of medicine Allergic diseases of the eye are chiefly conjunctivitis and lid reactions, the former the so-called vernal conjunctivitis, and as such they are seldom responsible for failing sight, but allergic scleritis and uveitis are important causes for gradual loss of vision.

In tuberculosis, sections of the lesions in the uveal tract seldom reveal the tubercle bacilli

The most serious form of uveitis is sympathetic ophthalmia, which is probably due to sensitivity to uveal pigment Differential diagnosis of allergic uveitis depends on the presence of the inherited allergic state, the elimination of other more easily identifiable inflammations, such as leprosy, syphilis and sympathetic diseases, and finally identification of the offending antigen by means of allergy tests.

Retinal causes of diminished vision are numerous Diabetes affects the eye late in the course of the disease, particularly in the form of chorioretinitis, though undoubtedly some cataracts have diabetes as their cause Diabetes may be the cause of [illegible] it has started

[illegible]

Often the first ocular symptom is visual failure, and when this occurs the chorioretinitis is severe. It may take place in patients in whom the diabetes is under control. The usual therapy for diabetes is completely ineffective with respect to established retinal lesions.

In cardiovascular-renal disease both sudden and gradual visual loss occur. The former is especially associated with large retinal hemorrhages and the latter with arteriosclerosis and small hemorrhages and exudates. The eyegrounds reveal the changes of malignant hypertension as early as these changes are to be found anywhere in the body.

Degenerative changes frequently accompany old age. The retina suffers in this condition primarily from malnutrition and probably an accumulation of waste products. Glaucoma causes a failure of vision

Optic atrophy is a major reason for failing sight. Among its most important medical causes are syphilis, hypophyseal tumor, multiple sclerosis and drugs. In these diseases the ophthalmologist is often the first to make the diagnosis. In 8 of each 10 patients who have supratentorial neoplasms, choked disks are present, whereas in those who have hypophyseal tumors atrophy of the papillomacular bundle is the rule. In multiple sclerosis the onset may be associated with optic neuritis, but more often there is simply temporal pallor of the nerve head with loss of central vision.

Failure of sight from optic atrophy may be sudden, as from poisoning from drugs such as methyl alcohol (CH_3OH) (see Methyl Alcohol, Chapter 19).

Peripheral field changes may be advanced before they attract the patient's attention, as for instance in chronic simple glaucoma, the most frequent cause of failing vision and blindness of middle and old age. This disease may not cause pain or redness of the eyes and is noticeable only to a discerning patient by a diminution in the visual field or halos about lights. Cataracts are common, and their role in failing vision is well known.

Congenital Color Blindness. Congenital color blindness or congenital color amblyopia occurs in 3 or 4 per cent of boys and men and in about 0 3 per cent of girls and women The condition generally affects both eyes and is often hereditary. The functions of the eyes are otherwise normal There are a number of tests for color vision which are particularly useful in the examination of employees in certain occupations in which perfect color perception is essential, for example in railway, steamship and aviation services as well as in motor driving. In transportation services the most commonly used signals are red and green, the colors in which most color-blind persons are defective.

There are a number of well-known tests for color vision· Stilling's test, Ishihara's test and Holmgren's test

The Holmgren test is frequently used, and is very convenient It employs a large assortment of colored worsteds This collection includes (1) test colors: pale green, light pink and bright red, (2) match colors lighter tints and darker shades of test colors and (3) confusion colors. yellow, brown, gray, drab, fawn, mauve, pale blue and the like. The test is performed in good daylight. The pale green sample is given to the individual, who is asked or required to select colors that match the test sample If he does this correctly, he has normal color sense If he not only fails to select similar colors but also confuses colors and in addition shows a certain hesitancy, his color sense is defective. Next a pink skein is selected and the person being examined is asked to match it. If, besides similar skeins, he selects blue or violet, he is red blind If he selects green or gray, he is green blind Finally he receives the bright red test skein for matching. If besides red, he chooses green and brown colors, darker than the red, he is red blind. If he selects shades of those colors lighter than the red he is green blind

Effect of Teaching on Color Blindness. Some men can be taught how to correct for color blindness Educational programs for those who are color blind have been conducted which permit them to pass tests for color blindness In one technic (Lepper) the subjects are instructed to get someone with normal color vision to assist them and to trace the shapes of the figures carefully even in those charts in which they can see the figures fairly well. They are instructed to continue working on harder and harder charts. Thus the person concerned builds a learning curve and with sufficient time seems to master the color manual It seems quite likely that those who have disturbances of color vision do fix in their minds appearances which are associated with certain colors when viewing objects that have for them some familiarity.

Alterations in the Field of Vision. The alterations in the size and shape of the visual fields which may be of value in diagnosis are hemianopsia, contraction of the visual fields for light, and contraction of the color fields. In connection with hemi-

anopsia, blindness due to disease of the optic nerve or its central connections is diagnostically important.

The diseases which may affect the optic tract are neoplasms, syphilitic meningitis, gummas and tuberculous meningitis. In these cases the crus may be implicated, causing hemiplegia or, as the result of basal lesions, ocular muscle paralysis may be present. The absence of any form of aphasia in right hemiplegia is against a central lesion and in favor of an affection of the optic tract

Hemianopsia. A condition termed hemiopia, hemianopia or hemianopsia is blindness of one half of the field of vision.

Since in the majority of cases of hemianopsia there is organic disease of the brain, hemiplegia and hemianesthesia on the same side with the hemianopsia are uncommonly associated symptoms; and, in left-side lesions, aphasia. If athetosis coexists with lateral hemianopsia, it is significant of a lesion involving only the posterior gray mass of the optic thalamus. If the hemianopsia involves a quadrant and not a semicircle, or is otherwise incomplete, and if mind blindness or word blindness coexists, the lesion is usually cortical. Dimness of vision in one eye, and a marked contraction in the visual field of the other, together with mind blindness (seeing but not recognizing objects), is a combination indicative of a lesion of the angular gyrus.

Hemianopsia in rare instances may be due to hysteria, in which case the conjunctiva is usually anesthetic and hemianesthesia is present. But by far the commonest alterations of vision in hysteria are contraction of the visual fields and changes in the color sense. The ophthalmologist can usually definitely distinguish the contraction of the visual fields due to hysteria from those due to organic disease.

Total blindness of one eye may be due to a lesion of one optic nerve, or disease of one occipital lobe, and if in addition there is hemianopsia of the opposite eye, it may be due to disease of the decussating fibers in the center of the chiasm together with the direct fibers of one lateral angle If there is no disease of the retina or other ocular structures sufficient to account for the loss of sight, a lesion at the decussation is likely to be present Total blindness of both eyes will be caused by disease affecting the entire chiasm, or bilateral lesions of the cuneus.

Hemianopsia, or blindness of one half of the visual field, is of different varieties and, together with the qualifying terms employed, the name refers to the field of vision from the point of view of the patient—not to the retina. Thus right temporal hemianopsia means that the outer or temporal half of the field of vision of the right eye is blind, so that if the eye is fixed on a point directly in front, objects to the right of the point of fixation will not be perceived. Therefore, remember that blindness of the temporal half of the field of vision is due to loss of function of the inner or nasal half of the retina, because of the crossing of the light rays in the media, and so with other varieties.

If the hemianopsia affects both visual fields, it is *bilateral*, if corresponding halves (both right or both left) are implicated, it is *homonymous* or lateral If both temporal or both inner fields are implicated, it is *heteronymous*. Furthermore, the inner fields are termed *nasal;* the outer, *temporal*. Very rarely the upper or lower halves of the visual field are effaced and if so, the condition is then called superior or *inferior* hemianopsia Hemianopsia may be partial, only a portion of the half field being blank. The unaffected half may retain its normal dimensions or, as in some cases, be reduced in size.

The presence of hemianopsia may be detected by those untrained in ophthalmology, but delineation of these defects is a task for the ophthalmologist To detect the presence of hemianopsia, each eye must be tested separately, the resting eye having been covered by a card. The patient, being placed with his back to the light, is told to fix the uncovered eye on that part of the physician's face (placed about 2 feet (61 cm.) away) which is most nearly on the horizontal plane of the eye to be

ested. The finger or a bit of white paper is then brought, first from one side, then rom the other, to the median line. If the patient cannot see the paper until it has assed nearly or quite to the line of fixation, hemianopsia exists. The vertical extent of the field is tested in a similar manner by bringing the object from above downward and from below upward

The diagnostic indications of the various forms of hemianopsia are as follows·

UNILATERAL NASAL HEMIANOPSIA. Blindness of the nasal half of the field, an extremely rare occurrence, indicates a very limited lesion at the outer angle of the chiasm.

BINASAL HEMIANOPSIA. Also rare is blindness of the nasal half of both fields, requiring for its manifestation two symmetric lesions, of both outer angles of the chiasm, or the outer sides of both optic nerves

BITEMPORAL HEMIANOPSIA. Blindness of the temporal halves of both fields is produced by a lesion involving the anterior angle or central portion of the chiasm.

The disease (affecting the chiasm) which is most frequently responsible for the three preceding varieties of hemianopsia is tumor or enlargement of the pituitary body, with which may be associated diabetes insipidus, proptosis and a flow of fluid from the nostril Other causes are tubercles, tumors, cysts, basilar meningitis, periostitis, exostosis, fracture of the body of the sphenoid bone, and gumma The last may give rise to evanescent recurring hemianopsia. When the chiasm is affected, the lesion is likely to be progressive, and gradually involves both crossed and uncrossed fibers, thus causing total blindness of one or both eyes, according to the extent of the destruction. Lesions of the chiasm may be attended by symptoms indicating involvement of the olfactory and trigeminal nerves and of the nerves of the ocular muscles, namely, anosmia, anesthesia of conjunctiva and cornea, and ocular paralysis

RIGHT OR LEFT LATERAL (HOMONYMOUS) HEMIANOPSIA Blindness of the right or left half of both fields is significant of a lesion situated at some point between the chiasm and the cortical center in the occipital lobe, namely, the optic tract, the pulvinar or posterior gray mass of the thalamus, the anterior corpora quadrigemina, the fibers passing from the thalamus and corpora to the occipital lobe either in the internal capsule or the optic radiations, or the cortical center itself

Contraction of the Visual Fields for Light. In order to determine the presence of this symptom, the examiner invokes the aid of an ophthalmologist and his perimeter, as it cannot be ascertained by any less accurate test. Leaving out of consideration glaucoma, optic atrophy or other organic disease, by far the most important indications of a nearly uniform contraction of the visual fields relate to the presence of hysteria and traumatic neuroses.. As a rule, one field presents a greater contraction than the other. In neurasthenia, while there may not be a true concentric limitation of the visual field, yet the fatigue of continued testing will sometimes develop a decided temporary diminution in its size

Contraction of the Visual Fields for Color. The color fields are tested by the perimeter, using bits of colored paper Passing from the circumference to the center of the field, the perception of white objects is found to have the widest extent. A little nearer, blue is perceived, then red, then green

Limitation of the color fields is a common symptom in hysteria and traumatic neuroses Sometimes a transposition of the normal fields for different colors will occur. Like vision in general, the color perception may be much reduced or abolished by optic neuritis or atrophy.

Amblyopia and Amaurosis. *Amblyopia* is a reduction in the acuteness of vision, a dimness or partial blindness, and cannot be relieved by glasses The condition is not dependent on any visible changes in the eye. *Amaurosis* is a total loss of

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Obstruction or thrombosis of the central artery causes a sudden loss of vision, commencing at the circumference of the visual field and extending to the center. It

is frequently indicative of cardiac or vascular disease, namely, bacterial endocarditis, valvular disease, particularly mitral stenosis, atheroma of the large arteries, aneurysm of the aorta, and thrombosis of the pulmonary vein; very rarely it occurs in rheumatic fever and chorea. In a very small proportion of cases the sudden loss of sight in chronic nephritis is said to be due to this accident or to separation of the retina

The most frequent causes are uremia, diabetes, and certain drugs, large hemorrhages, migraine and hysteria When occurring in uremia, loss of sight ordinarily follows coma or convulsions, is sudden and usually lasts but 1 or 2 days. Quinine and the salicylates may cause sudden amaurosis, and it sometimes occurs in alcoholism Severe hemorrhages, particularly those from the stomach, may be responsible for a sudden failure of sight Migraine may exhibit as one of its symptoms a fugitive blindness, perhaps of only one half the visual field (hemianopsia). The amaurosis of hysteria is associated with emotional states and other characteristic symptoms, and no matter how complete the apparent loss of sight may be, the pupillary reflex, both direct and consensual, is retained

Hysterical amblyopia usually affects young girls and women and occasionally boys and young men. This form of amblyopia is most often bilateral, but it may be unilateral. The most constant symptom is reduction in vision amounting to complete blindness The field of vision is contracted concentrically both for white and for colors The pupillary reflexes and ophthalmologic examinations reveal no abnormalities

Simulated amblyopia is a resort of malingerers, who frequently pretend various degrees of loss of vision in one or both eyes in attempts to recover damages for lesser injury The tests for simulated amblyopia are difficult to perform, because the claimant often has been coached in the various devices of evasion, such as closing one eye and then the other during the test in order to ascertain which eye is being examined The ophthalmologist is aware of all of these difficulties.

Blindness in both eyes is more difficult to detect than blindness in one eye Contraction of the pupil to light is presumptive evidence of some sight, but in rare instances the pupils react to light in total blindness In malingering, when a claim of blindness is made, the ophthalmologist, by the use of special tests with lights and prisms, can detect evidences of eyesight

Night blindness or *nyctalopia* is a condition in which the sight is good by day, but deficient at night Sometimes there is a history of exposure to bright light. It may accompany certain forms of atrophy of the optic nerve such as that manifested by retinitis pigmentosa Night blindness may result from a deficiency of vitamin A. Xerophthalmia is often present at the same time

Hemeralopia is a condition in which the patient sees better in an obscure light than in bright sunlight

Ocular Manifestations of Malaria. Malarial amblyopia occurs as a result of the action of the malarial toxin on the optic nerve and retina Often optic neuritis and papillary edema result from the blocking of the retinal and choroidal vessels by parasites and leukocytes. The retinal hemorrhages are usually small, multiple and peripheral; large macular hemorrhages do occur in the malignant types of malaria. Ulceration of the cornea is a common ocular sequela of malaria, and recurrent iritis is frequently associated with this keratitis. The complaints are loss of vision, frequent headaches in the occipital and temporal regions, dizziness, pain in the eyeballs, tenderness on palpation, photophobia, lacrimation, and spots before the eyes

The objective findings are irregularity of the pupils, retinitis of the atrophic type, usually in or around the macular area, unusual concentrations of choroidal pigmentation, generalized hyperemia of the retina and nerve head, optic neuritis both mild and severe, optic atrophy, and in a few cases a severe progressive chorioretinitis and uveitis

Refraction and Errors of Refraction. In the normal eye light passes through media of different densities, being refracted at the surfaces of junction of the media so

that the incident ray comes to focus on the retina. This condition is termed emmetropia.

If the incident parallel rays come to focus anterior to, or before they reach, the retina, the condition is known as myopia or nearsightedness.

In hyperopia, hypermetropia or farsightedness, there is a lack of refracting power sufficient to bring to focus the incident or parallel rays of light on the retina.

Myopia. The common cause of myopia is an abnormally long anteroposterior diameter of the eyeball which results in the condition termed axial myopia. Curvature myopia results from aberrations in the curvatures of the refracting surfaces of the cornea and lens which bring the incident light rays to a premature focus Abnormal positions of the lens may create similar difficulties. Myopia may arise when the refractive indices of the cornea, aqueous humor or the lens are changed significantly.

Myopia is rare in the newborn, but its incidence increases rapidly until the age of about 20 years is attained Its incidence has no relation to any uses of the eye, but excessive use of a myopic eye is deleterious. The cause of myopia is some predisposition which provides the requirements for myopia to develop.

In myopia a crescentic posterior staphyloma (myotic crescent) in the fundus of the eye is present and this development is seemingly of congenital origin. This sort of staphyloma is associated with some distortion of the papilla.

In mild or low myopia there is indistinct distant vision. In more severe or high myopia there is indistinct vision and discomfort after near work as the result of disproportion between the efforts of accommodation and convergence. The eyes are sensitive to light Black spots are seen floating before them, and sometimes flashes of light are noticed. Flashes of light before the eyes are often a symptom too of detachment of the retina In very high myopia the eyes are prominent, the pupils are large, and the anterior chamber appears deeper than normal, probably only owing to the dilatation of the pupil. There may be an apparent convergent squint. A true divergent strabismus may be found, either concomitant or affecting only one eye. Vision may be very poor, even with correction, scotomas may be present, both central and peripheral

The ophthalmologist usually reports normal findings on ophthalmoscopic examination of the myopic eye In moderate myopia there is a myopic crescent. If there is a high error of refraction, a posterior staphyloma is recorded, often with a change in the course of the retinal vessels, and degenerative changes in the choroid—a chorioretinal atrophy There may be described hemorrhages in the macular region. Vitreous opacities and a black spot at the fovea may be present Detachment of the retina is likely to occur in a myopic eye

With a refractive error of up to 5 or 6 diopters myopia, unless in children of preschool age, has a good prognosis If there are 10 diopters or more of myopia the prognosis is not good Serious retinal damage or detachment of the retina is likely to ensue

Hypermetropia (*Hyperopia*). Hypermetropia is almost always present in the infant Its incidence decreases rapidly during the first two decades of life.

In many, especially the young, with ample reserve powers for accommodation there are no symptoms unless the condition is extreme. When the powers of accommodation are insufficient from any cause, there ensues eye strain. The eyes, after use, ache, feel dry and require excessive blinking. Rarely there may be lacrimation

In aging persons the far point is beyond the range of comfortable reading The print has to be held farther away than usual in order to read at all. In the aged the hypermetropia is index hypermetropia and much of the deficient vision may be due to an increased refractive index at the cortex of the lens.

The conjunctivae and edges of the lids become reddened. Headache, often frontal, follows excessive use of the eyes. Ophthalmoscopically the fundus may exhibit no abnormality A bright reflex is commoner in hypermetropic than in

emmetropic or myopic eyes. The inferior crescent and an abnormal tortuosity of the retinal vessels are common in hypermetropic eyes. In some cases there is a pseudopapillitis

Astigmatism. Astigmatism is present when there is defective curvature of the refractive surfaces of the eye as a result of which a ray of light is not sharply focused on the retina. The light is spread over an area of the retina and not brought to a focus on a spot of the retina. There are many varieties of astigmatism. Each variety is named according to its causation by prefixing an appropriate adjective or adjectives for instance, corneal astigmatism, which is due to irregularity in the curvature or refracting power of the cornea.

Regular astigmatism designates the condition in which the refractive power of the eye shows a uniform increase or decrease from one meridian to another, being practically constant in each meridian, and the image produced is regular in shape, either a line or an oval or a circle

Regular astigmatism is likely to cause the worst forms of asthenopia or eye strain, the asthenopia in these cases is only in part accommodative. It is often worse in the lower degrees of astigmatism than in the higher. Aching of the eyes, severe headaches and migraine are matters for complaint. The eyes become fatigued easily. The letters of print run together

Anisometropia. A slight anisometropia is almost the rule. It is a condition in which the refraction of the two eyes shows a difference. In mild forms of anisometropia binocular vision is imperfect In high-grade anisometropia binocular vision can be obtained only by the use of correct lenses. Distinct vision, even with correction, may be only uniocular and the eye which is not in use may become divergent In some instances if one eye is emmetropic, the other myopic, the emmetropic eye may be utilized for distant vision and the myopic eye is used for near vision.

Anisometropia is usually of congenital origin. The symptoms are variable and may not be noticeable to the child

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5

TOPOGRAPHY AND REGIONAL DIAGNOSIS OF DISEASES OF THE NECK

The neck, by means of the cervical vertebrae and muscles, elevates the head and allows it to be moved freely in different directions. It is interposed between the portals of entry to the respiratory and the digestive system and the thoracic organs. It is therefore subjected to secondary invasions by the agents of infectious diseases as well as the extension of malignant processes from both directions. In addition the neck may be involved in disease arising in its own organs. Some of the diseases are of congenital origin. The majority of the congenital diseases, such as branchiogenic and thyroglossal duct cysts, are remnants of vestigial organs.

In this portion of the text are considered the structures of the neck in the median line, those regions, or triangles, on each side, anterior to the sternocleidomastoid muscle, those posterior to this muscle, between it and the trapezius (Fig. 5-1), and finally the air passages.

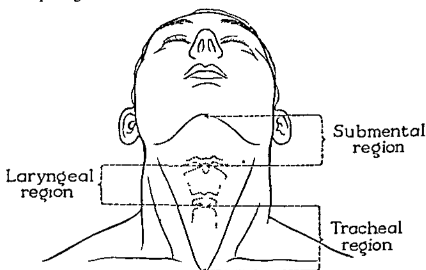


Fig 5-1 Median regions of the neck

REGIONS OF THE NECK

Median Portion. Viewed from in front, the median portion of the neck may be divided into three regions, submental, laryngeal and tracheal

The *submental region* extends from the chin to the lower border of the body of the

The *tracheal region* extends from the lower edge of the cricoid cartilage of the sternum. Just above the sternum, between the sternal origins of the sternocleidomastoid muscles, is the suprasternal notch. Laterally the region is limited by the sides of the trachea.

Triangles of the Neck. The ventral and lateral aspects of the neck are divided into anterior and posterior primary triangles by the sternocleidomastoid muscle. The base of the anterior triangle is the border of the jaw, and of the posterior triangle the clavicle. The anterior cervical triangle is secondarily divisible into three small triangles: the *submaxillary*, between jaw and digastric muscle; the *superior carotid*, bounded by digastric, ... *rior carotid* (or muscular) *tri-* ... rior cervical triangle is divided ... *ccipital* and *omoclavicular triangles*. Each of these triangles is at times further subdivisible into minor regions (Fig. 5-2).

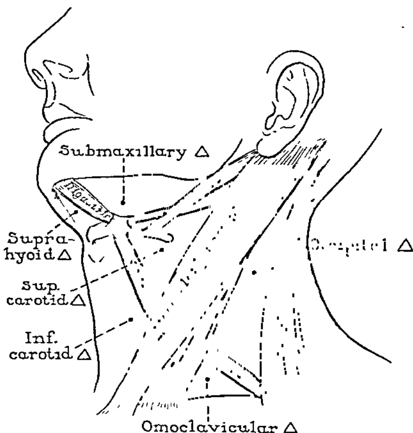


Fig 5-2 Triangles of the neck.

STRUCTURES TO BE FELT IN THE MEDIAN LINE

Some necks are short and stout, others are medium in length and thickness, others are long and thin, and there are many gradations between these types. For this reason it sometimes may be easy, sometimes difficult, to identify the structures.

On palpating downward from the symphysis of the mandible, the finger discerns a hollow. On pressing into this hollow, the finger rests between the digastric muscles on each side and on the mylohyoid muscles beneath. Still deeper than the mylohyoid muscles are the geniohyoid and geniohyoglossus muscles attached to the genial tubercles on the inner side of the mandible. If the lymphatic nodes at this point are enlarged, they can be felt

The hyoid bone is next and it can be readily felt in the median line. If it is not easily discovered in the median line, it can be felt by a finger and thumb placed on each side of the neck above the thyroid cartilage.

Passing over the hyoid bone, the finger sinks into the space between the hyoid bone and the top of the thyroid cartilage. Next comes the thyroid cartilage or Adam's apple. This structure can readily be seen in adult males and in thin persons of either sex. Despite obesity it can always be felt. The finger then sinks into the space between the thyroid cartilage above and the cricoid cartilage below.

From the cricoid cartilage, which is on a level with the sixth cervical vertebra, down to the sternum only soft structures can be felt. The sternum projects forward and the trachea inclines backward so that opposite the top of the sternum the trachea is about ¾ inch (2 cm.) behind the sternum. The distance between the top of the sternum and the cricoid cartilage in an adult male is about 1¾ inches (4.5 cm.) The trachea may be brought closer to the anterior portion of the sternum by overextending the head

If palpation is limited strictly to the midline, only the isthmus of the thyroid can be felt However, it is well to remember that the thyroid gland sometimes enlarges during menstruation and always somewhat during pregnancy, returning to the normal size during the interval

A tumor in close relations with the trachea, and moving with it during the act of swallowing, is an enlarged thyroid gland A solid, hard enlargement is usually a simple goiter, and the enlargement ordinarily is greater on one side than on the other Determination of the presence or absence of induration and of fluctuation, pulsation and systolic thrill and murmur is routine during physical examination of the gland

If fluctuation is present, the enlargement is in all probability a cyst, either of the thyroglossal duct or of the thyroid gland. If pulsation, thrill and murmur exist, the *case is one of exophthalmic goiter. If a diffuse enlargement with tenderness* is present, an acute or subacute thyroiditis is the cause.

Tumor or aneurysm in the root of the neck and behind the sternum may cause prominence of the thyroid

The thyroid gland in some conditions of disease undergoes *atrophy*. Often in myxedema and cretinism the thyroid is impalpable

Abnormal situation of organs in the neck often indicates disease; for instance, displacement of the trachea to one side or the other may be due to chronic fibroid phthisis, thoracic aneurysm, or mediastinal tumor. In pulmonary tuberculosis the trachea is drawn to the affected side by the shrinking lung. Aneurysm of the innominate artery pushes it to the left

Tracheal tugging is considered a valuable sign in cases of suspected mediastinal tumors or aneurysms In aneurysms it depends on the fact that the arch of the aorta curves back over the left bronchus, and if an aneurysmal dilatation of the arch is present, each systolic distention of the vessel presses down on the bronchus, thereby pulling the trachea downward

To determine the presence of tracheal tugging, if the patient is ambulatory, stand behind him and have him close his mouth and raise his chin The tips of the forefingers are then placed firmly on either side of the cricoid, pressing upward; then if a downward tug is present, it will be detected

MUSCLES OF THE NECK

The sternocleidomastoid muscle is the one muscle of the neck that lends itself for examination. If the patient is lying down, have him raise the head; or if sitting up, turn the head as far as possible to the right and left, with or without resistance offered by applying the hands to the sides of the head; or bend it forward against pressure on the forehead. If the muscle is not paralyzed, it stands out prominently (Fig. 5-3); nerve supply, the spinal accessory nerve (eleventh cranial nerve).

Torticollis or Wryneck. Torticollis or wryneck, a disorder in which the neck is so twisted that the face is turned toward the side opposite the contracted muscle

and looks somewhat upward, usually is caused by some disorder of the sternocleidomastoid muscle. The sternocleidomastoid is not always the only muscle involved, for the trapezius and others often are affected likewise, owing to an attempt of the other cervical rotators to sustain and relax the sternocleidomastoid and thus obtain physiologic rest for it. When the trapezius alone is involved, the head is drawn backward and toward the affected side.

Torticollis is congenital or acquired. The congenital form is caused by injury to the sternocleidomastoid muscle occurring at birth or to developmental defects of atlas, occipital bone or cervical ribs. A swelling or tumor may be present in the course of the muscle when the muscle has been injured at birth. In the acquired form the distortion may be more or less permanent and may be due to caries or other disease of the spinal column. In such cases it is evident that treatment is to be directed to the diseased spinal column rather than to the sternocleidomastoid muscle, which is found to be relaxed

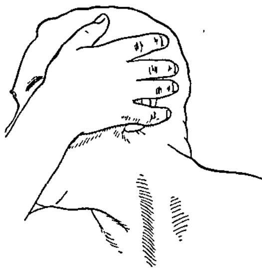


Fig 5-3 Sternocleidomastoid muscle Attempts are made to rotate the head against resistance Nerve supply, spinal accessory nerve (eleventh cranial nerve).

Inflammation of muscles, fascia or the lymph nodes of the neck may cause the patient to hold the head and neck in a distorted position, *wryneck*. The wryneck in such cases will disappear as the cause subsides Rheumatic affections, "taking cold in the neck," are a common cause of torticollis in which the sternocleidomastoid muscle may become contracted.

A chronic torticollis occurring in an adult may be conversion hysteria.

Spasmodic Disorders. *Nodding spasm,* a rhythmic nodding movement of the head and neck, may be a form of habit spasm. If nodding spasm is accompanied by a momentary loss of consciousness, the condition is epilepsy. Nodding spasm may be indicative of hysteria, either alone or as a part of a rhythmic or hysterical chorea (salaam convulsion). Pulsating shaking of the head seemingly arising in the neck is often seen in the aged, and occasionally in persons with aortic insufficiency.

Spasmodic jerking of the head, recurring every few minutes, in which the head is brought toward one shoulder, and at the same time the face is rotated to the opposite side and the chin raised, is the clonic form of spasmodic torticollis The shoulder may be simultaneously jerked upward to meet the head In chorea the movements of the head are by contrast extremely irregular and bizarre, and the facial muscles are affected before those of the neck.

DISEASES DUE TO PRENATAL INFLUENCE

Tumors of the Thyroglossal Duct. The vestigial rests of the thyroglossal duct account for some of the midline tumors of the neck. These tumors lie between the isthmus of the thyroid gland and the base of the tongue. Most commonly they occur either below or above the hyoid bone A remnant of the thyroglossal duct may end at the hyoid bone, but should it continue upward, it may pass in front of, through or behind the body of that bone.

Thyroglossal cysts are independent of the thyroid gland A cyst of the thyroglossal duct is manifested by a gradually developing, painless enlargement in the

front of the neck. If unsuccessful attempts have been made to remove the cyst, most can be learned from the history prior to surgical operation. Before there has been infection or surgical intervention, both the tumor and the skin over the cyst are movable.

Cysts occur also just beneath, within or on the dorsum of the tongue. When they are large, there may be disturbance of respiration as well as of deglutition. These cysts may become malignant.

Thyroglossal cysts may become infected and may suppurate from time to time, apparently healing completely, to discharge again in a few years without having been operated on. From such repetitions of suppuration, sinuses may result.

The exact diagnosis of cyst of the thyroglossal duct can be made only by microscopic study of the tissues

Branchiogenous Cysts and Fistulas. *Branchiogenous cysts* commonly occur in the upper part of the anterior triangle of the neck, just beneath the angle of the jaw. They develop slowly. In the beginning these tumors are benign but they may become malignant while yet of small size. In the early stage a branchiogenous cyst is not apparent unless the skin is stretched over it. A tumor of this type can attain a large size, displace the sternocleidomastoid muscle backward, and bulge in the floor of the mouth at the base of the tongue

Branchiogenous fistulas are persistent gill-cleft remnants remaining as ducts which extend from near the floor of the mouth to the skin in the region of the insertion of the sternocleidomastoid muscle around to the midline. The whole of the duct or only part of it may be persistent. If one of these fistulas is not patent at one end or at both ends, it is a cyst and is called a gill-cleft cyst.

There is a history that the tumor opened spontaneously or by incision and that since its opening there has been a draining sinus. There is a small inflamed tumor medial to the sternocleidomastoid muscle If a sinus is present, it may drain continuously or it may become closed for some time, to reopen anew.

When one of these fistulous openings is explored with a probe, it can be followed for varying distances in the direction of the floor of the mouth The probe may even pass the entire length into the oral cavity

The diagnosis is made by microscopic study of the tissue

Dermoid Cysts. Dermoid cysts are small midline tumors of the neck which appear under the chin The patient usually complains of a bulge under the chin like the chin of an obese individual These tumors often bulge into the floor of the mouth, or they may appear almost entirely within the mouth on each side of the tongue. Other situations in the neck for dermoid cysts are near the mastoid process, or the cysts may protrude from the mediastinum in the episternal notch.

Diagnosis is established by microscopic study of the tissues.

Angiomas. There are congenital hemangiomas and lymphangiomas of the neck

Hemangiomas occur rarely in the cervical regions They usually are situated in [illegible] ...ay be deeply set in the tissues and may not be [illegible] These tumors often do not increase in size, but [illegible] hemangiomas communicate with the venous system and consequently they are compressible, as soon as the pressure is removed they reappear Some of these tumors are large and produce extensive bulging over the lower part of the neck Generally, however, they are limited to the skin or to the superficial tissues

Diagnosis is established by the behavior of the tumor on application of pressure. The tumor disappears on pressure and returns immediately on release of the pressure.

Lymphangiomas are common lesions of the neck which often are situated beneath the lower jaw and gradually attain a large size, filling the entire side of the neck. They occur also in the supraclavicular fossae, and in the axillary and the

femoral regions Occasionally a lymphangioma may extend into the mediastinum. As a result of irradiation these tumors may appear to be diffusely inflamed and, under these circumstances, are difficult to differentiate from neoplastic disease.

The diagnosis is established by microscopic study of the tumor tissues.

LYMPHADENITIS OF THE NECK

One of the commonest affections of the neck is inflammation of the lymph nodes. The term lymphadenitis formerly was employed in descriptions of tuberculosis and syphilis. The term as used here includes all infections of lymph nodes.

The acute infections of the lymph nodes are caused by one or more of the pyogenic microorganisms, *Spirocheta, Borrelia, Treponema* or a filtrable virus. In the great majority of cases these acute infections of the lymph nodes subside and are designated as nonsuppurative lymphadenitis A nonsuppurative lymphadenitis is a regular concomitant of tonsillitis and other acute bacterial infections of the mouth. Enlarged lymph nodes from viral infections do not suppurate.

In infections of the mouth the lymph nodes in the drainage area of the mouth become enlarged and sensitive to pressure. The reaction of the lymph nodes is usually obscured by the reactions of the causative disease. The inflamed nodes may themselves produce general symptoms after the original causative lesions have subsided However, the manifestations of an acute lymphadenitis usually are limited to tenderness due to the inflammation of the capsule of the lymph node and to perinodal edema. If the infection is severe, the capsule of the node may be invaded, and if a number of nodes are involved, the inflammation may extend beyond the capsule so that the individual nodes cannot be made out

The situation of the involved nodes depends on whether the infection is situated in the mouth or in the throat The enlargement of the nodes may be progressive along the line of drainage; that is, first those near the site of infection enlarge and become tender; then they subside, to be followed by enlarged nodes in more remote regions The involvement of the lymph nodes in remote regions of the neck, or diffuse involvement, is usually indicative that infection is not in the mouth. Infection of the scalp, the fingers, arms and, occasionally, of the axilla may cause an enlargement of the lymph nodes in the neck At times it may seem that the acute inflammation of these cervical lymph nodes is going to terminate in suppuration, the edema and cellular induration having formed a diffuse mass, but almost always the lesions subside spontaneously

Acute Diffuse Lymphadenitis (Ludwig's Angina) Extension of the inflammation in an infected lymph node beyond the node or its capsule constitutes diffuse lymphadenitis Occasionally, diffuse lymphadenitis will develop in the neck as a result of some severe infection in the oral cavity, and this acute diffuse infection tends to follow the planes of the fascia in the neck This condition, if severe, is known as Ludwig's angina Ludwig's angina usually is confined to the floor of the mouth, and because the tissues become very hard and woody, the condition is known as woody phlegmon or ligneous phlegmon, which later extends to the neck. At times Ludwig's angina may be extremely acute and may terminate fatally within a very short period, 1 or 2 days.

Viral Lymphadenitis. Many of the viral infections and infectious mononucleosis are accompanied by preaural and cervical enlargement of lymph nodes

Chronic Lymphadenitis. The lymph nodes, subsequent to an acute or an unrecognized inflammation, may become chronically enlarged and be palpable as discrete nodules

In the presence of chronic lymphadenitis it is important to determine whether tuberculous infection exists and to differentiate it from other types of chronic lymphadenitis The beginning of tuberculous lymphadenitis is usually in the superior

triangles of the neck There is no acute onset. The nodes become enlarged slowly.

Tuberculous Lymphadenitis. Tuberculous lymphadenitis is commoner in children than at other ages, but it occurs frequently enough in young adults In an occasional instance of tuberculous lymphadenitis the lymph nodes break down and a sinus results Even in these cases recovery tends to occur spontaneously and often completely

In some instances, in those in a weakened condition, tuberculous lymphadenitis develops rather rapidly The development is slow in those who have good health.

In the beginning of tuberculous lymphadenitis the nodes are discrete but they tend to become matted together When these nodes remain discrete and are situated in the lateral triangles of the neck, there is a resemblance to the lymphoblastomas, especially of the Hodgkin type

Often a lesion is not suspected to be tuberculous until after it has been removed, cross section and microscopic study of the tissue then confirm the diagnosis.

Lymph nodes situated over the parotid gland are particularly likely to break down and to leave sluggish superficial ulcers. Once the skin is perforated, a chronic discharging sinus ensues.

Syphilitic and Mycotic Lymphadenitis. In former years it was taught that syphilis was a common cause of lymphadenitis of the neck. An enlargement of the lymph nodes in the posterior triangles of the neck, if the possibility of pediculosis capitis had been excluded, was considered to be almost pathognomonic of syphilis. It is now known, however, that there are many causes of subacute, chronic and indeterminate lymphadenopathies which include infections by bacteria, viruses or fungi, toxoplasmosis and diseases of unknown origin such as infectious mononucleosis

ULCERATIVE INFECTIONS OF THE NECK

Aside from ulcerating tuberculous lesions, the common pyogenic boil or furuncle, and fistulous tracts from congenital cysts, there are very few ulcerating lesions of the neck. Other than the lesions just named are those of the various fungi Blastomycotic ulcers on the neck usually are accompanied by ulcers elsewhere on the body, especially on the hands Sporotrichosis, likewise, which is common on the hands, may occur on the neck. Actinomycotic infection of the mouth or jaws may occasionally cause ulcerations of the neck Other uncommon causes of ulcers of the neck are Vincent's angina, leukemic tumors and abscess from the cervical vertebrae and dental infections

CAROTID SINUS SYNDROME

(*Vagal Syncope—Thomas Lewis, Nothnagel's Syndrome*)

The regulation of blood pressure is an autonomic proprioceptive reflex mechanism, which acts mainly by the intermediation of the pressoreceptor innervation of arterial and venous vascular areas (Weiss and Baker).

The bifurcation of the common carotid artery is richly supplied with sensory receptors which originate in the adventitia and leave the sinus as the sinus nerve to join the

n

can be responsible for attacks of unconsciousness and convulsions and that such attacks can be reproduced by slight trauma such as pressure over one carotid sinus The attacks are associated with cerebral anoxemia resulting either from cardiac asystole or from a primary reflex depression of the blood pressure. A hypersensitive state of the carotid sinus reflex may produce unconsciousness, convulsions or milder manifestations through one or more of three main reflex arcs The three motor pathways responsible for syncope involve the vagus nerve, the vasomotor depressor nerves or the central motor pathways. In a mixed form one or the other pathway may play the dominant role. In normal

subjects mechanical stimulation of the carotid sinus does not produce symptoms. The hyperactive carotid sinus reflex may be either unilateral, involving only one sinus, the activity of the other reflex remaining normal, or bilateral.

Three types of carotid sinus syndrome have been described. In the *vagal type* the symptoms, particularly the dizziness, fainting and weakness, result from cardiac asystole. The asystole is due either to sino-auricular or to auriculoventricular block, which in its turn produces acute cerebral anoxemia. In its pure form the afferent reflex travels over the vagus nerve to establish a heart block. The *depressor type* usually appears in association with one or the other two types The symptoms result from primary reflex vasodilatation and secondary depression of the blood pressure entirely unrelated to cardiac slowing or any form of cardiac arrhythmia. In the *cerebral type* the symptoms result apparently from impulses which travel directly to the brain. The attacks may be induced within as short a period as 5 seconds. Neither atropine nor epinephrine aborts or relieves the cerebral type of attack.

The loss of consciousness as a complaint may occur under diverse circumstances such as nervous upsets, claustrophobia, change in position, quick turning of the head, tight collar or blows on the neck. The reflex is more prevalent in men than in women. The frequency and degree of response increases as age advances. Coronary disease is the commonest condition in which the reflex occurs with the greatest frequency and the highest degrees of response.

The loss of consciousness may come on suddenly or gradually. There usually are pallor, sweating, severe weakness, nausea and sometimes dizziness with a sensation of falling The heart rate may drop, often to about 40, and the blood pressure falls rapidly The radial pulse is not palpable. The unconsciousness is of short duration; the patient is confused for a few minutes and weak for some time afterward. Sometimes following loss of consciousness a convulsive seizure ensues as in Adams-Stokes syndrome.

If a hypersensitive carotid sinus is suspected, an attack can be produced. Before inducing an attack, have the patient sit in a safe place to prevent injury in case he should fall. The attack is then precipitated by pressure or firmly stroking the area of the carotid sinus.

Vagovasal reflexes may bring about the same changes in some patients as those which follow swallowing with an inflamed or irritated pharynx or esophagus. The induced attacks are not dangerous but are unpleasant and, if frequent, cause nervous worry which probably favors more attacks. However, an occasional death has been recorded after artificial stimulation of the carotid sinus

These patients should have electrocardiographic studies to rule out a heart block before attempts are made to induce an attack or to stop an attack by the use of drugs. The attack should not be induced in any patient suspected of having an organic heart disease

PROTRUSION OF CERVICAL INTERVERTEBRAL DISKS

The sex distribution shows that affected males decidedly predominate. A history of trauma may occasionally be obtained. Before the appearance of symptoms of a medullary lesion, signs of cervical radiculopathy may be present.

The symptoms are extremely variable and resemble those of tumors and degenerative disease of the spinal cord Segmental symptoms, arising from root compression, may be present

The findings on physical examination are, like the symptoms, variable. In advanced protrusions of a disk the findings are those due to pressure on the spinal cord in this region Plain roentgenograms of the cervical portion of the spinal column may show extensive spondylosis deformans. Myelograms made by the injection of air into the cisterna magna reveal a subarachnoid space which is narrowed and distorted by an anterior protrusion, which reaches the spinal cord There

is no obstruction to the passage of the air into the thoracic subarachnoid space. In only a few cases will the protrusion be limited to one intervertebral disk.

TUMORS OF THE NECK

Tumors of the Carotid Bodies. These tumors are rare lesions which arise in the carotid bodies, which lie in the angle formed by the branching of the common carotid artery into its two branches. This angle is situated in the superior carotid triangle at a midpoint equidistant from the mastoid process, the angle of the jaw and the thyroid cartilage. Carotid tumors may develop, however, at considerable distances from this general situation. They may be bilateral and familial. These tumors grow very slowly, their development parallels that of the mixed tumors of the salivary glands. Pain transmitted to the region of the ear is occasionally present. In most of the rare instances of carotid tumor the growth is discovered when the neck is being palpated for lymph nodes. These tumors may become malignant; the chances are four in five, however, that they will remain benign.

Diagnosis is established by the presence of chromaffin cells at biopsy.

Ganglioneuromas. In Recklinghausen's disease (generalized neurofibromatosis) there are multiple tumors along the peripheral nerves all over the body. Some of these tumors may be situated in the neck. These multiple tumors, usually found in the deep midportion of the neck, grow very slowly (see Diseases of the Peripheral Nerves, Tumors, Chapter 6).

Diagnosis is suggested by the presence of Recklinghausen's disease but can be established definitely by biopsy.

Primary Cystadenomas. Cystic tumors of the neck comprise cystadenomas which arise in the lymph nodes, and cystic aberrant thyroid glands. The other cystic tumors which have been enumerated in the foregoing paragraphs are regarded as remnants of the gill clefts and cysts of the thyroglossal duct.

Lipomas and Myxomas. Lipomas of the neck are rare. They do occur in the lower and posterior regions. The myxoid tumors of the neck are more deeply seated generally than lipomas. However, good differentiation on palpation cannot be made between myxoid and lipomatous tumors.

Diagnosis is established by biopsy study.

Atheromatous Cysts. In common with dermoid cysts, atheromatous cysts or wens occur on the lateral surfaces of the neck, especially on the posterior portion. These tumors are definitely attached to the skin but their walls are distinct from the surrounding tissue.

Lymphoblastomas. *Lymphoblastomas of the Hodgkin type* involving the cervical lymph nodes are particularly difficult to differentiate clinically from tuberculosis. A common location of palpable lymph nodes in Hodgkin's disease is along and behind the midportion of the sternocleidomastoid muscle and in the supraclavicular fossa. These lymph nodes are often a conglomerate irregular mass, rather diffuse, tumor-like, and matted together. In Hodgkin's disease each lymph node maintains its independence, but the sense of touch may not interpret this individuality of existence of lymph nodes in a large mass which fills the whole region of the neck. If Hodgkin's disease is suspected clinically, often there are palpable nodes in the axillae and the inguinal regions because Hodgkin's disease or other diseases of the lymphoblastic group may arise first in these regions. The beginnings of Hodgkin's disease may be in the mediastinum or in the retroperitoneal lymph nodes, and the disease may be limited to these regions throughout its course, with very few nodes enlarged in the neck, axillary regions, or inguinal region. Hodgkin's disease may invade the skin.

Diagnosis of Hodgkin's disease is established by biopsy of a node.

The *lymphoblastomas of the sarcomatous type* are commoner in middle-aged men, whereas the lymphoblastomas of the Hodgkin type are commoner in young

men. Lymphosarcomas appear in the upper parts of the posterior triangles of the neck or just beneath the upper third of the sternocleidomastoid muscle. These tumors may begin in the anterior triangle of the neck and often in the supraclavicular fossa A common site of lymphosarcomas is in the mediastinum, where they are discovered by means of roentgenograms, usually after the tumors have invaded other tissues and some symptom is presented which requires roentgenologic examination of the thorax. Lymphosarcomas often invade the skin or the tissues surrounding them, and they grow rapidly.

Diagnosis is established by biopsy of an enlarged node.

Lympho-Epitheliomas (Endotheliomas) of the Lymph Nodes. A lympho-epithelioma usually appears at the angle of the jaw and often precedes or follows a pharyngeal tumor, a tumor of the cranial cavity, or a sinus. A characteristic feature of these tumors is that severe pain may attend the appearance of the initial enlarged node or even antedate its appearance.

Lympho-epitheliomas are fixed in position from the beginning These tumors are highly malignant, and the termination is an invasion of the neck and the mediastinum by direct extension

Diagnosis is established by biopsy of a lymph node.

Malignant or Secondary Tumors. Secondary tumors of the neck are metastatic tumors which occur within the lymph-drainage system from a primary malignant tumor and correspond in structure to the original tumor. It is not always possible to determine the site of the original tumor.

For the most part, however, the secondary malignant tumors of the neck are carcinomas that have originated on the lips, tongue, gums, floor of the mouth, nasopharynx, face or scalp In carcinoma of the stomach, testicles or kidneys there may be a small fixed lymph node—*Virchow's node* or sentinel or signal node—superior to the medial end of the left clavicle.

Melano-epitheliomas may occur on the lip or in the neck; they metastasize to all parts of the body. Metastatic tumors in the regions of the neck are prone to become secondarily infected from the oral cavity, irrespective of the site of origin

DISEASES OF THE PHARYNX

The mouth, the larynx, the esophagus, the two eustachian tubes and the two posterior nares open into the pharynx, which thus serves as the common tract for intake of air, food and drink.

Pharyngeal Openings The opening of the *mouth* into the pharynx sometimes is narrowed from cicatricial contractions resulting from ulcerative processes such as syphilis, and from burns due to swallowing of caustics. There rarely is obstruction downward, so that patients with such narrowing usually can swallow, but the cicatrices contract the opening upward, and the soft palate, its arches and the walls of the pharynx may be bound together in one cicatricial mass, preventing respiration through the nose

The opening between the *larynx* and the pharynx is easily accessible to those experienced in the procedure of examination If the tongue is drawn well forward, the tip of the epiglottis can be seen, and if a long straight tongue depressor is used, in many cases [illegible]

[illegible]

of the foreign body is in the larynx and part in the pharynx A foreign body can often be dislodged if the finger is thrust its full length into the mouth and throat and swept from side to side

The opening between the *esophagus* and the pharynx is in a line with the long axis of the pharynx. The opening of the larynx, on the contrary, is more on the anterior wall of the pharynx. It is for this reason that a tube introduced either through the mouth or through the nose passes into the esophagus and usually does not enter the larynx Excep-

tions to this rule occur more frequently in comatose patients in whom the tube passes more freely into the larynx.

The *eustachian tube* passes from the anterior portion of the tympanic cavity downward, forward and inward to the upper posterior portion of the pharynx The eustachian orifices, one on each side, are on a level with the floor of the nose. The upper border of the pharyngeal opening is approximately ½ inch (1 27 cm.) above the soft palate and about an equal distance below the basilar process. The lateral third of the eustachian tube, near the ear, is bony and the inner two thirds are cartilaginous. The isthmus of the tube is at the point of junction of the bony and cartilaginous portions and is the narrowest portion of the tube. The tube opens in swallowing and yawning and admits air to the tympanic cavity and mastoid cells. Interference with this process may cause the so-called aviation otitis with retraction of the ear drum during aeroplane trips. Catarrhal affections of the throat readily travel up the tube and set up an inflammation of the middle ear Swelling of the lining of the tube follows and air no longer passes to the ear.

The eustachian tubes are often involved in acute or chronic infections of the throat and middle ears The commonest symptoms related to eustachitis is popping and roaring noises in the ears These noises may be enhanced by or synchronous with the pulse beats.

The *posterior nares* open into the upper portion of the pharynx above the soft palate. This portion, the nasopharynx, differs from the oral and the laryngeal parts of the pharynx in that its cavity always remains patent.

Pharyngeal Diverticula. In pharyngeal diverticula the pouch opens into the pharynx by a transverse opening in the middle line about 1 inch (2 5 cm) in length The orifice varies in size in different cases and may be merely a slit. The pouch makes its passage between the pars obliqua and the pars fundiformis of the inferior constrictor immediately above the mouth of the esophagus There are two hypotheses as to the origin of these diverticula. the first, that they are due to embryologic defects; the second, that the cause is mechanical The theory that there is weakness in this region that is due to some sort of prenatal influence, concerned in the formation of either type of pouch, probably is correct

The symptom that is always constant in a pharyngeal pouch is the return of fragments of undigested food. This return is not immediately after the food has been taken, but many hours or even days afterward Solids are more troublesome to swallow than liquids, there is no dysphagia but the patient has to make two efforts before deglutition is accomplished. Abnormal secretion of saliva and difficulty in disposing of it may be the only sign in elderly persons. There is no vomiting or pain, but the patient may notice a gurgling noise in the throat, especially when lying down and at meals; this noise is followed by the bringing up of quantities of phlegm.

The diagnosis depends on the presence of fullness in a posterior triangle of the neck on which pressure produces a gurgling noise and the escape of gas into the mouth. The opening into, and the diverticulum itself, may be demonstrated by roentgenologic and endoscopic examinations.

Pharyngitis. The mucous membrane of the nasopharynx is ciliated columnar; that of the lower portion of the pharynx is squamous The mucous membrane contains racemose mucous glands and follicles or crypts surrounded by lymphoid tissue, and it is well supplied with blood vessels. The pharynx is frequently affected by inflammation or pharyngitis An abnormal general redness of or discrete eruptions [illegible] mucous [illegible] ta, ery- [illegible] ay also be seen. So also with petechiae, infarcts and extravasations of blood or bleeding surfaces.

When the lymph follicles are markedly involved, they can be seen studded over the posterior wall of the pharynx This constitutes follicular pharyngitis. Not infrequently some ulceration may be present, forming ulcerative pharyngitis. Should abscess formation occur around the pharynx, arising from an infection from the oral cavity, the pus occupies the retropharyngeal space between the buccopharyn-

geal fascia and prevertebral fascia. Its spread upward is limited by the skull; laterally, by the sheath of the carotid vessels; hence it passes downward behind the esophagus and may enter the posterior mediastinum.

The Pharyngeal Tonsil (Adenoids). The pharyngeal tonsil, composed mainly of lymphoid tissue, extends across the posterior wall and roof of the pharynx between the eustachian tubes.

Hypertrophy. The pharyngeal tonsil when enlarged hangs from the vault of the pharynx. It is a somewhat lobulated mass, and when large, in children, obstructs nasal respiration Under these conditions the disease known as adenoids is present. Mouth breathing results, and the child is likely to snore and make other queer respiratory sounds when sleeping These children may literally fight for breath at night.

A child who has reached 3 or more years of age and has marked adenoids presents a typical appearance The mouth is open, the lips are thick, the upper lip is elevated, the teeth project, the chin recedes, the alae nasi are atrophied and tense from want of use, and the nasal orifices are reduced to elongated slits. The philtrum is indistinct, and disuse of the muscles between the upper lip and the eyes gives the face a flat, smooth, characterless expression. Most such children have a more or less constant discharge of mucopus from the anterior nares, leading to excoriation and eczema of the upper lip The nose, however, in some cases may be dry. The adenoidal child often breathes noisily, owing to obstruction. The voice is often without resonance The most important secondary affection of adenoids is the effect on the organs of hearing According to some observers, almost one third of these children have some defect in hearing The facial expression may remain after the adenoids have been removed and persist into adult life.

Retropharyngeal Abscess. Retropharyngeal abscess may arise from any one of three causes: cervical caries, suppuration of lymphatic nodes, or extension of pus from the middle ear through the canal for the tensor tympani muscle Retropharyngeal abscesses occur external to the pharyngeal aponeurosis and bulge into the throat. Because of the looseness of this aponeurosis and its lack of firm attachments, these abscesses may not bulge forward as a distinct circumscribed swelling. They are more likely to gravitate downward and hang in a loose baglike manner opposite the base of the tongue They are too soft to be easily felt. They are more easily discovered by inspection In the search for the etiology of retropharyngeal abscess roentgenologic examination of the spinal column is made to detect the possible existence of spinal caries or Pott's disease, and the ear is examined for suppurative otitis media

Diseases of the Pharynx Due to Disturbances of Innervation or Psychic Control. *Anesthesia* of the pharynx is associated with hysteria and is indicative of some interference with the sensory functions of the glossopharyngeal and vagus nerves It is found in diphtheritic neuritis, hysteria and bulbar paralysis. Globus hystericus is a functional disorder of the ninth nerve

Spasm of the pharyngeal muscles on attempting to swallow is a functional affection of the motor portions of the same nerves It may be present in neurotic and hysterical individuals, in hydrophobia, true or false, in tetanus and in strychnine poisoning. It is probably an element in globus hystericus.

Paralysis of the pharynx, if bilateral, causes difficulty in swallowing, the food is not passed into the esophagus, and portions may enter the larynx. If the paralysis is unilateral, there is little if any difficulty in deglutition Pharyngeal paralysis indicates an involvement of the nuclei of the ninth and tenth cranial nerves or of the nerves in their course, as in bulbar paralysis, Landry's paralysis, and neuritis, or in basal lesions, as meningitis, tumor or aneurysm

Malignant Growths. Malignant disease is rare as a primary affection of the pharynx It is usually secondary to direct propagation in the last stage of cancer of

the larynx, the base of the tongue, a tonsil or the esophagus. Either carcinoma or sarcoma may occur; the former is the commoner.

In malignant disease in the region of the pharynx the patient at first complains of discomfort in the throat and interference with speaking, swallowing and nasal respiration Sharp pains develop early and extend to the neck, ears or angle of the jaw. Pain of burning character in the ear is a common symptom.

On examination there often is observed the presence of frothy mucus or saliva in one or both of the pyriform fossae. With the increase of the growth the voice may be hoarse, and respiration is observed to be seriously interfered with There are salivation, dysphagia, blood-stained sputum, foul breath and enlargement of the regional lymph nodes

The age of the patient, the one-sided affection, spontaneous pain and progress of the disease suggest the diagnosis It is established by biopsy study of tissue removed.

DISEASES OF THE LARYNX

The larynx is composed of the large epiglottis, the thyroid cartilage, the cricoid cartilage and three pairs of small cartilages

In the infant the larynx is situated opposite the second, third and fourth cervical vertebrae In the adult it has descended to the level of the fourth, fifth and sixth cervical vertebrae

The uppermost part of the epiglottis is below the dorsum of the tongue Extending forward from the epiglottis to the base and the sides of the tongue are three glosso-epiglottidean folds In the fossae formed by these folds, foreign bodies such as capsules, tablets and fish bones may become lodged Objects lodged here are easily seen by aid of the laryngoscopic mirror

The vocal cords lie immediately behind or just below the most prominent portion of the anterior edge of the thyroid cartilage, which commonly is called the Adam's apple

Examination of the Larynx Examinations of the larynx and the lingual tonsil to be of value require skill and considerably more knowledge of the procedures than can be gained by casual interest and an occasional attempt to make such an examination

The laryngologist may report the presence of swelling, ulceration or tumors on, above, or below the vocal cords In tuberculosis multiple ulcers may be seen Syphilitic or cancerous ulcers are usually described as single ulcers In the ordinary forms of laryngitis the vocal cords are said to be of a gray-pink or reddish color, and pinkish nodules may be present on the edges of the cords A failure of the cords to move properly, or paralysis, may be reported

Laryngeal Paralysis. Paralysis of the muscles of the larynx is rarely, if ever, due to cortical disease, but is caused by lesions affecting the nuclei or origin of the vagus in the medulla or the nerve itself at some part of its course Thus it may be implicated at its origin by the lesions of bulbar paralysis, syringomyelia, locomotor ataxia or multiple sclerosis, or an injury, tumor or disease of the base of the brain may involve the nerve near its superficial origin The causes of paralysis most frequently encountered are those which affect the vagus nerve or its laryngeal branches in the neck or the thorax, namely, in the neck, enlarged cervical lymph nodes, enlarged thyroid gland, tumors of the neck or the pharynx, and caries of the cervical vertebrae; in the thorax, aneurysm of the aorta, abscess, tumor, or enlarged lymph nodes in the mediastinum, esophageal cancer and, rarely, compression resulting from inflammation of the pericardium or pleura and pulmonary tuberculosis. The nerve and its branches may become inflamed (neuritis), or the laryngeal muscles themselves may undergo pathologic changes terminating in paralysis as an effect of the toxins of a number of the acute specific infections, notably diphtheria; or chronic poisoning, especially from lead and alcohol.

Total bilateral paralysis is most commonly indicative of aneurysm of the thoracic aorta, cancer of the esophagus, great enlargement of the thyroid, or mediastinal tumor.

Abductor paralysis is commonly unilateral and is the most frequent variety of laryngeal palsy.

Adductor paralysis, either bilateral or unilateral, is as a rule of functional origin.

Paralysis of the *interarytenoid muscle* (adductor) is most likely to be a symptom of hysteria.

Paralysis of the *internal thyro-arytenoid muscles* (adductors) is a not uncommon result of overuse of the voice and laryngeal inflammation.

The Voice (The Faculty of Speech). A loss of voice or whispering voice (aphonia) and coarse or harsh quality of the voice (hoarseness or dysphonia) are both due to some interference with the function of the vocal cords. Abolishment of action of the cords may be due to local and inflammatory disease of the larynx or to disease of or pressure on the recurrent laryngeal nerve Aphonia may come suddenly or be preceded by hoarseness, or the latter alone may be present.

In the majority of cases aphonia and hoarseness are due to some form of laryngitis, such as the acute or chronic catarrhal variety associated with acute infections of the upper part of the respiratory tract, syphilis or tuberculosis Edema of the glottis and retropharyngeal abscess are occasional causes Excessive use of the voice or excessive cigarette smoking may induce congestion of the cords, and cause hoarseness or aphonia Tumor of the larynx, impacted foreign bodies and cicatricial stenosis of the larynx may be found responsible.

Disorders of Speech from Involvement of the Laryngeal Nerves. The larynx receives its nerve supply from the superior and inferior laryngeal branches of the vagus nerve. Interference with their functions gives rise to anesthesia of the larynx or paralysis of the laryngeal muscles, manifested by aphonia, hoarseness and, if the abductors are affected, dyspnea.

If there is a deep, hoarse voice and a brassy cough, with a tendency for particles of food to enter the larynx, there is probably interference with the superior laryngeal nerve, giving rise to anesthesia of the upper portion of the larynx and paralysis of the cricothyroid muscles This interference is often due to bulbar paralysis, a peripheral neuritis, or the pressure of a tumor such as a goiter or carotid aneurysm.

If there is aphonia without cough or dyspnea, it may be due to paralysis of all the laryngeal muscles caused by bulbar paralysis, tumors of the medulla, diphtheria, or pressure on both recurrent nerves; or to complete paralysis of the adductors, which is usually of functional origin, but may occur from overuse of the voice or laryngitis.

Hoarseness, with easy fatigue on slight use of the voice, is indicative of unilateral abductor paralysis, of which the commonest cause is a mediastinal tumor or an aneurysm pressing on one recurrent nerve If right-sided, it may be due to a much thickened pleura, cancer of the upper part of the esophagus or mediastinal tumor.

A modified but understandable voice and phonation may be maintained in the presence of a dangerous laryngeal paralysis resulting from locomotor ataxia, bulbar palsy or pressure from a tumor or aneurysm

A rattling, rough voice, the so-called ventricular voice, is due to the occasional vicarious vibration of the false vocal cords or ventricular bands in cases in which the true cords are paralyzed or destroyed by ulceration. Other abnormalities of the voice consist in a double or triple splitting of the sounds In the first variety the two sounds, although simultaneous, differ in pitch (diplophonia, diphthongia); this phenomenon is due to a small tumor on the edge of one vocal cord or to unilateral paralysis of the cords The triple voice is very uncommonly observed and is caused by a pedunculated tumor which has its attachment below the vocal cords. During

the early portion of phonatory expiration the growth rises, the voice is clear; during the middle part it lies between the cords, the voice is of normal tone but of decreased volume; and during the latter part the tumor has been protruded to a point above the glottis and the voice is clear.

The peculiar quality of voice which goes by the name of nasal voice is sometimes a matter of habit and lack of training of the voice. It is of service to recognize two varieties of the nasal voice. The first, the *open nasal*, is caused by nonclosure of the nasopharyngeal opening by the soft palate and may be imitated by speaking without opening the mouth, the second, the *closed or stopped nasal*, is due to nasal stenosis, and resembles the tone imparted to the voice by speaking while the nose is pinched between the thumb and forefinger.

The open nasal tone is indicative of a congenital cleft of the palate, of paralysis of the soft palate, or destruction of the soft palate. The closed nasal voice is often present in coryza, hypertrophic rhinitis, nasal polyp or postnasal adenoids.

Dumbness or *mutism*, inability or unwillingness to speak, may be present in hysteria, idiocy, melancholia and dementia Feigned inability to speak is sometimes resorted to by malingerers. A real inability to speak may be due to cerebral fatigue which succeeds a severe and exhausting illness, particularly severe fevers. Mutism exists in those who are congenitally deaf, or in children who become totally deaf before the power of speech is permanently acquired.

Anarthria, indistinct or imperfect speech, the impairment varying in extent, may be an evidence of paralysis of the tongue, soft palate and facial muscles. Glossitis, parotitis and the absence of teeth may be responsible for a mumbling manner of talking

A *slow, interrupted* manner of speech, the words being slurred over, somewhat as if the patient were intoxicated, with tremulousness of the tongue and lips, is observed in general paresis and myxedema

A *piping, querulous* voice, with manifest hesitation in beginning a sentence, the words then being rapidly spoken, is characteristic of paralysis agitans.

Scanning speech, in which the words are spoken slowly, each syllable accented as if reading verse, is an important symptom of multiple sclerosis but is also found in Friedreich's (hereditary) ataxia.

These disturbances of the voice may be of such nature that their final diagnosis and differentiation require a consideration of the faculty of language

The Faculty of Language. Normal Speech Mechanism. The normal exercise of the faculty of language depends on the existence and integrity of certain cerebral centers (1) psychic centers of intelligent perception, (2) sensory receptive centers, (3) emissive or motor centers and (4) the association tracts Finally, there are the basal ganglia for the special senses and the nuclei in the medulla and spinal cord actuating the muscles employed in articulate speech, which constitute respectively the sensory and motor peripheral apparatus

Apraxia. If an individual has varying degrees of defects in the power of recognizing or understanding the nature and uses of objects or, possibly, the identity of persons, the condition is termed apraxia The varieties of apraxia correspond in number and character to the varieties of sensations. mind blindness, mind deafness, mind anosmia, mind ageusia and mind atactilia.

Apraxia is closely allied to, and is often found in connection with, the various forms of aphasia, that is, an inability to produce or understand spoken or written speech (see The Nervous System and Locomotion, Chapter 6).

Aphasia and Its Varieties. The term aphasia embraces a variety of defects in the use or in the comprehension of language, either spoken or written. In order to understand and interpret this symptom and its several forms a conception of the *normal* manner and mechanism of the faculty of language is desirable. The subject is complex, and many exceptional and often unexplainable cases occur. As far as

possible the statements made here are those the truth of which is considered as probable.

MOTOR OR ATAXIC APHASIA. This variety embraces as its most important division *aphemia*, the loss of power to utter words, although the patient knows what he desires to say, because he cannot revive the motor memories for articulating them. Occasionally these patients may be able to sing even though they fail in attempts to talk. This sort of aphasia is common to most aging persons—those 50 years or more of age—in a mild form *Agraphia* is inability to write words for lack of power to recall the motor memories of the muscular actions involved in writing.

SENSORY APHASIA. The principal varieties of sensory aphasia are the auditory and visual. *Auditory aphasia* or word deafness is, as its name indicates, an inability to recognize words when spoken The patient hears, but does not understand, as if listening to a foreign language *Visual aphasia* or *alexia* is a condition in which the patient sees, but does not recognize or understand written or printed words. *Memory aphasia* consists of inability to recall the sound of a word or phrase. Once the sound is recalled, the word or phrase can be spoken. This is a form of sensory aphasia incident to aging

EXAMINATION FOR APRAXIA AND APHASIA. To determine the presence of *word deafness* (auditory aphasia), the examiner must elicit the information indicated by the following questions.

1. Can sounds be heard by the patient? Ability or lack of ability to hear determines the presence or absence of ordinary deafness
2. Can spoken words be heard by the patient? If so, then
3. Can the spoken words be understood? This may be ascertained by having the patient put out the tongue, open and close the hand A failure to comply indicates inability to attach any meaning to the words, and word deafness is present, which is the principal symptom of auditory aphasia

To determine the presence of *word blindness* (alexia, visual aphasia):

4 Can the patient see objects?
5. Can written words be read?
6 Can written or printed words be understood? This may be ascertained by writing out a question, or a direction, for instance, "Close your eyes." A failure to comply indicates word blindness, which is the principal symptom of visual aphasia

To determine the presence of *motor aphasia* (aphemia)·

7. Can the patient speak voluntarily?
8. Can words be repeated?
9 Can the patient read aloud? If unable to do these things, motor aphasia or aphemia is present

To determine the presence of *agraphia*

10. Can the patient write?
11. Can dictation be written?
12. Can a sentence or words be copied? If he is unable to do these things, agraphia, a symptom which may be found in all forms of aphasia, is present. If the patient is unable to write voluntarily because of inability to remember words or their appearance, but can write to dictation, the disability is sensory agraphia. If it be impossible to write either voluntarily or to dictation, a motor agraphia is present

To determine the presence of *mind blindness*

13. Are ordinary objects recognized and their uses known? Put before the patient two or three familiar objects and question him about one of them. If the proper article is not picked up, the subject has mind blindness, provided that inability to understand the request is owing to word deafness

To determine the presence of *mind deafness*.

14 Does the patient recognize ordinary sounds, that is, does the ring of a bell, the ticking of a watch, awaken a recognition of its import? If not, the patient has mind deafness.

There are variations in the degree of all the speech defects There may be only a

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tracheitis, acute obstructive laryngotracheobronchitis, and an unclassified noninfectious croup due to allergy, foreign body and chemicals or other irritative agents). The presence or absence of supraglottic edema and the position and motion of the vocal cords before and after suctioning of the subglottic area and trachea have furnished a dependable guide to the choice of therapy

Here the interest is in spasmodic croup

Spasmodic croup is a form of laryngeal stridor of unknown etiology, characterized by sudden onset and unaccompanied by fever It affects children, more commonly boys than girls, between the fourth month and the end of the second year of life. The attacks may continue until the child is approximately 10 years of age.

The disease affects feeble, undernourished children who often have nasopharyngeal adenoids, enlarged faucial tonsils, enlarged bronchial lymph nodes and disorders of the upper air passages

The child as a rule goes to sleep as usual He suddenly is awakened from a sound sleep struggling for breath. The forced effort at inspiration produces a croupy, crowing stridor. In the effort to fill the lungs the child sits up in bed, tosses his hands about, holding to the nearest support or clutching his throat All the accessory muscles of respiration are thrown into action. The mouth is open, the nostrils are dilated and the chest is heaving, but as all these efforts fail to fill the lungs, the diminished pressure causes retraction of the lower ribs and the manubrium sterni. The expression is one of terror as the patient becomes cyanotic. The head is thrown back and the child is soon covered with sweat In severe attacks respiration may cease for a few seconds In such cases there are carpopedal contractions, convulsions and even involuntary passage of urine and feces The attacks are usually of short duration, often less than a minute, and rarely do they exceed 2 minutes. The attack is ended by one long, deep, relieving inspiration Relief from the attack is followed by a croupy cough. Further attacks may take place during the same night, and they often recur from night to night for some time After the attack the child falls asleep and the next morning his health is as usual.

The diagnosis of this condition is not difficult if it is remembered that the paroxysms characteristically begin with sudden onset and without fever and hoarseness and end as abruptly as they begin

Syphilis. Ulcers of syphilitic origin may involve almost any portion of the larynx but they usually are anterior and involve the epiglottis. These ulcers often are associated with syphilitic manifestations in the mouth which are ulcers that are most marked posteriorly, blanching of the mucous membrane of the mouth and the presence of a white frothy mucus The serologic reactions for syphilis are positive

Stenosis. Acute laryngeal stenosis is met with in wounds, injuries, foreign bodies, acute laryngitis, septic inflammation, diphtheria, membranous laryngitis, the exanthems and syphilis. It has been known to occur rather suddenly in tuberculosis of the larynx

The chief symptoms of laryngeal stenosis are dyspnea, stridor, and alteration or extinction of the voice All of these symptoms are intensified on exertion. The patient prefers to sit up in bed, for breathing seems easier in this posture It is remarkable how hard a patient may be striving for air in this condition and yet be free from marked cyanosis

The diagnosis is established by laryngoscopic examination.

Laryngeal Symptoms of Nervous Origin. The laryngeal symptoms in mediastinal tumor are due to irritation of, or pressure on, the vagus nerve or its recurrent laryngeal branches There are cough, attacks of dyspnea and alterations in the voice. In the irritative stages the cough is paroxysmal, hoarse, imperfect and brassy. When one or both recurrent branches are completely paralyzed, the cough loses its sharp, ringing character and becomes hollow and blowing.

partial loss of any one of the normal powers of expression, depending mainly on the extent of the productive lesion.

DISEASES WHICH CAUSE APHASIA. In the majority an aphasia is one of the symptoms of organic focal cerebral disease, occurring in the left hemisphere in right-handed persons, and vice versa. The localization and appraisal of aphasia is the work of the neurologist. Aphasia may occur as the result of a cerebral hemorrhage, thrombosis, embolism, abscess or tumor.

In rare instances aphasia occurs in hysteria and neurasthenia and epilepsy. It is an occasional symptom in migraine, and may be present during convalescence from severe and exhausting fevers

Infections of the Larynx. ***Acute Laryngitis.*** Acute laryngitis is an acute catarrhal inflammation of the mucous membranes of the larynx manifested by hoarseness or aphonia and occasionally by cough The acute inflammation may primarily attack the larynx, whence it spreads downward to the trachea and bronchi or upward to the nose. Frequently the laryngitis is but an extension downward of an acute catarrh of the nose or the pharynx. Or, rarely, an acute inflammation first develops in the bronchi and spreads upward to the larynx. The attack often is precipitated by excessive and, more particularly, improper use of the voice It may follow on the vomiting and retching of an alcoholic debauch, an attack of seasickness or a passionate attack of crying or sobbing

In the early stages of acute laryngitis the visible changes in the larynx may be very slight, but as the hoarseness increases, the signs of inflammation increase proportionately

When uncomplicated, an acute laryngitis is without danger and subsides within from 3 to 10 days

Chronic Laryngitis. Chronic laryngitis is a catarrhal inflammation of the mucous membranes of the larynx, characterized by an impairment and alteration of the voice Disorders of the nasal and the postnasal cavities and, to a less extent, of the pharynx and mouth are the most potent factors in originating chronic laryngitis. The alteration of the voice is at first an intermittent huskiness, but when the symptom is well established, the hoarseness is persistent; it is more marked after a rest or on arising in the morning than at other times and tends to disappear after a little use of the voice The tone of the voice is lowered; aphonia is seldom complete, except after prolonged or extreme forcing of the damaged organ A sense of fatigue and soreness of the throat may be present. There is frequent clearing of the throat by hemming and hawking

On physical examination the mucous membrane is congested. The vocal cords may be only slightly affected but often appear dull and gray.

The diagnosis usually is not difficult for the examiner who is trained in inspecting the larynx. Because tuberculosis of the lung may be accompanied by a chronic and inveterate laryngitis. care should be taken to exclude the possibility of this disease

Nodular laryngitis is a form of chronic laryngitis generally caused by faulty use of the voice and characterized by local thickening of the vocal cords The symptoms are those of chronic laryngitis. The diagnosis is madé by one who is accustomed to inspect the vocal cords and larynx.

The laryngologist may describe other forms of laryngitis such as (1) hypertrophic laryngitis and (2) chronic atrophic laryngitis

Laryngismus Stridulus or Spasmodic Croup. Gilbert and associates have called attention to the multiplicity of names for croup and offer the following classifications. (1) diphtheritic croup with three subgroups (diphtheritic obstructive laryngitis, laryngotracheitis and laryngotracheobronchitis) and (2) nondiphtheritic croup with five subgroups (acute catarrhal laryngotracheitis, supraglottic edematous obstructive laryngitis, subglottic obstructive exudative and edematous laryngitis and

CARCINOMA OF THE VOCAL CORDS Four of each five laryngeal cancers arise on the vocal cords. Cancer of the vocal cords is almost always either squamous cell carcinoma or papillary carcinoma The low inherent malignancy of these neoplasms in the presence of poor lymphatic drainage of the true cords renders carcinoma arising on the cords likely to remain localized for a considerable period of months, occasionally longer.

The cardinal and only early symptom of carcinoma of the vocal cords is hoarseness Hoarseness in middle-aged or aging men which persists for more than 2 weeks requires inspection of the larynx.

A general physical examination does not reveal any significant findings so long as the laryngeal tumor is limited to the structure Early evidence of extension is recorded by the otolaryngologist as immobility. Only in extensive spread will there be any palpatory evidence present

All lesions of the larynx are examined for evidence of syphilis.

Examination of the thorax may aid in differential diagnosis in regard to tuberculosis and syphilis Roentgenograms of the larynx may be helpful in indicating the site of origin, position, and extent of laryngeal tumors

Biopsy is necessary to establish the identity of any proliferative or ulcerative lesion of the cords. Benign papillomas may cause confusion, even on microscopic examination. Repeated biopsies are occasionally necessary There is no evidence to indicate that carefully performed biopsy on the vocal cords increases the danger of spread of cancer.

Surgical treatment is the preferred procedure when the lesion is limited; otherwise radium may be used

Leukoplakia Laryngis. Leukoplakia of the larynx is characterized by white thickenings of the upper surface of either or both of the vocal cords that appear much the same as the patches of leukoplakia of the tongue Leukoplakia laryngis can be diagnosed only by a physician of a great deal of experience in examinations of the larynx.

DISEASES OF THE TRACHEA

Acute Tracheitis. Acute tracheitis is usually a part of the common cold, although in some instances an acute infection seems to be limited to the trachea

The symptoms of acute tracheitis vary in intensity, and the duration is comparable to that of acute bronchitis The symptoms consist of hoarseness, cough and perhaps fever and ineptitude The diagnosis is by inference if the patient promptly recovers the voice and if the cough and the fever cease

Chronic Tracheitis. A chronic tracheitis, often of severe grade, frequently arises from a long-continued inhalation of irritating fumes or dusts or from excessive tobacco smoking Chronic infection of the paranasal sinuses, mouth, nose and throat, when the discharges are aspirated into the trachea, frequently results in chronic tracheitis and bronchitis

An endoscopic examination may be necessary as diagnostic proof if the rest of the respiratory system is normal

Tracheal Stenosis. Irritating gases, corrosive fumes, and acute and intense infections may cause stenosis of the trachea, which may reach such a degree as to result in severe dyspnea and extreme cyanosis. This often occurs during the course of an ordinary bad cold

Tumorous growths inside or pressure from outside the trachea may cause a chronic, slowly progressive stenosis. Trauma and slowly progressive infections such as that of syphilis also may produce stenosis

Rupture of the trachea, usually due to the trauma of instrumentation, as a rule is fatal When tracheal rupture occurs from trauma of other origin, the condition

In tabes dorsalis there may be laryngeal anesthesia, paresthesia or hyperesthesia. The symptoms are described respectively as tickling, irritation, and tightness or a sensation of choking. The voice becomes thick and jerky, owing to ataxic movements of the cord. Laryngeal crisis often occurs in the early stage and may precede other signs of the disease by several years The laryngeal crisis and spasmodic attacks vary much in intensity and frequency; they seldom cause death by asphyxia

Other diseases of the nervous system which may affect the larynx are disseminated sclerosis, bulbar palsy, dystrophia myotonica (myotonia atrophica), myasthenia gravis and syringomyelia

The diagnosis is suspected when there are attacks of dyspnea, alterations in the voice, and cough during the course of the aforementioned diseases

Laryngeal Vertigo. Laryngeal vertigo (laryngeal syncope, laryngeal epilepsy) occurs in middle-aged neurotic men who are suffering from laryngitis, bronchitis, bronchial asthma or pulmonary tuberculosis The attack begins with laryngeal tickling or irritation, followed by a short cough, spasm of the larynx, dyspnea, transitory syncope and slight convulsive movements Such attacks may recur every day or at intervals of a month or more

Laryngoscopic examination is impossible during the attack and the findings are negative in the interim The diagnosis is made from the history and the presence of an obvious psychoneurosis Serious deterioration of health may follow the onset of laryngeal vertigo.

Tumors. Benign Tumors. Benign tumors of the larynx are comparatively rare In this group the *papilloma* is the commonest It occurs earlier than any other type of benign tumor, and may be congenital Nearly all laryngeal growths met with in infants and in children up to the age of 10 years are of this character.

CYSTOMA Pathologically cysts of the larynx are due to retention from obstruction in the duct of a muciparous gland Their commonest situation is on the anterior surface of the epiglottis

OTHER BENIGN TUMORS Lipoma is a rare tumor of the larynx, as are angioma, adenoma, myxoma, lymphoma, neurofibroma and tumor of the thyroid gland. The last-named tumor, which may arise from abnormal distribution of thyroid tissue, is extremely rare and of relatively little importance.

LARYNGEAL POUCH This pouch is conveniently referred to here because it clinically resembles a benign tumor, although its pathologic origin is uncertain. Laryngeal pouch, the so-called prolapse of the ventricle of Morgagni, is a membranous sac between the superior vocal cord and the thyroid cartilage On examination a smooth, pink, fleshy growth with a broad base is seen issuing from the ventricle of Morgagni and resting on the vocal cords

Malignant Tumors. Both carcinomas and sarcomas occur in the larynx In appearance and symptoms carcinoma and sarcoma of the larynx are so much alike that biopsy must be performed to establish the diagnosis

Carcinoma of the larynx may occur without involvement of the vocal cords, or these structures may be primarily affected

Lesions of the larynx which do not involve the vocal cords have their origin in the epiglottis, the false cords, the ventricular cavity, or the subglottic area. These lesions cause virtually no early symptoms, and are usually not discovered until there is pain, extensive infiltration of cartilage and muscle, or metastasis to the regional lymph nodes With the occasional exception of lesions localized on the tip of the epiglottis, pain is seldom a complaint until the disease is well advanced and then pain often is severe, extending to the ear and the side of the head and being much increased by swallowing. Respiratory obstruction is marked when these intrinsic lesions advance. There may be pharyngeal symptoms and interference with deglutition. These lesions may not be amenable to resection but many are radiosensitive.

During the active secondary stage of syphilis, changes in the trachea and bronchi may occur, resulting in symptoms of an acute tracheitis or bronchitis. Mucous patches develop, and in the tertiary stage gumma is sometimes seen in the trachea and bronchi. Cough is usually the first symptom of this condition The gumma may be absorbed, so that the cough does not become productive. If ulceration occurs, however, considerable mucopurulent sputum is produced From such ulcers there often is blood-streaked sputum or even frank hemorrhage. These ulcers occasionally extend through the wall of the trachea or a bronchus and invade the adjacent structures, such as the mediastinum, the esophagus and even the pulmonary artery. Stenosis of various degrees results in difficulty in respiration, even to the point of terminating fatally. In such cases the physical findings, including results of roentgenologic examination do not differ from those caused by stenosis from other causes.

Diagnosis is sometimes assisted by the detection of syphilitic disease, or its scars, in the nose, pharynx, or larynx, but in many cases these aids are not forthcoming, and then the cause of the stenosis is arrived at by inspection, or by endoscopy.

The prognosis will depend on the degree and the depth of the stenosis. In cases in which the contraction is low down, or cannot be relieved, or extends into the bronchi, the outlook is very grave

Syphilis of the Lungs. O'Leary was able to prove the diagnosis of syphilis of the lungs in only 6 instances over a period of 20 years

Syphilis of the lungs is so rare that the symptoms are unknown

The diagnosis is made by exclusion There are nodular infiltrated lesions in the upper pulmonary fields, positive results of serologic tests of the blood and negative results from other diagnostic laboratory procedures A therapeutic test for syphilis is said to confirm a presumptive diagnosis when the symptoms disappear, roentgenologic examination shows that the lesions in the lungs have disappeared, and the patient gains weight and comments on how well he feels The serologic reactions of the blood do not show any significant change until many years later.

Tumors. ***Benign Tumors.*** The benign growths of the trachea are papilloma, fibroma, lipoma, adenoma, hemangioma and lymphoma, lymphadenoma, mixed parotid tumors, osteoma, enchondroma, and aberrant thyroid tissue tumors Papillomas and fibromas are, as in the larynx, the commonest. Papillomas of the trachea, the most frequent growths of all, are generally extensions from the larynx, and hence occur in young children Fibromas come next in frequency.

If the growth is in the trachea, symptoms may be noticed only when there is considerable stenosis The patient usually first complains of dyspnea. This may occur suddenly and fatally The voice is usually enfeebled, though not lost. Hoarseness will depend on the degree to which the vocal cords are involved by catarrh Simple neoplasms of the bronchi generally attract attention in the first place by causing hemoptysis Dyspnea is not severe, but obstruction to the escape of secretions from the lung produces cough and expectoration of infected sputum, sometimes of fetid character

The effects are mechanical, owing to lack of aeration and drainage of the lung beyond the point of obstruction The neoplasm in such case may occlude the trachea. It may, however, if pedunculated, be pulled down during inspiration and cause obstructive emphysema by its reversed check-valve action

If there are manifestations of obstruction of the trachea, information may be gained by roentgenography

Amyloid Tumors of the Larynx and Trachea. The larynx and the trachea are common sites of localized deposition of amyloid. Amyloid tumors of the larynx, trachea or bronchi may occur in association with amyloid degeneration elsewhere in the body or as isolated deposits The isolated deposits, according to New, may be divided into (1) diffuse subepithelial infiltrations, (2) tumor-forming amyloid deposits, and (3) amyloid degeneration in a pre-existing tumor

usually is not suspected because of the other serious symptoms resulting from the trauma. Spontaneous rupture rarely occurs Tracheo-esophageal fistula is fortunately rare. These fistulas cause severe respiratory distress and dysphagia

In summary, all of these conditions, namely, acute tracheitis, chronic tracheitis, tracheal obstruction and stenosis, and tracheo-esophageal fistula, may be diagnosed clinically. However, roentgenoscopic and bronchoscopic confirmations are obtained when warranted by the conditions

Acute Laryngotracheobronchitis. Acute laryngotracheobronchitis occurs in children and in the aged *Streptococcus hemolyticus* and *Hemophilus influenzae* are causative organisms There is a sudden onset of cough, dyspnea and cyanosis. A tenacious and thick, later purulent, exudate is coughed up. The tenacious secretions may obstruct bronchial ramifications and thus produce atelectasis Mediastinal emphysema and spontaneous pneumothorax may result from overdistention of the alveoli. On examination of the chest there are noisy coarse rales but no changes on percussion or in the breath sounds.

The diagnosis is established by the history and the physical findings. Roentgenoscopic examination in either children or the aged differentiates this condition from bronchopneumonia

Ulcerative Tracheobronchitis. The tracheobronchial ulcerations may result from recurring attacks of atypical pneumonia, bronchiectasis, abscesses, tuberculosis, sarcoidosis and fungous infections The characteristic symptom is persistent cough with considerable blood-streaked sputum which occasionally contains gross blood Fever and loss of weight or failure to gain weight are often present Examination by physical means usually gives negative results

The diagnosis is established by seeing the ulcerations with the bronchoscope The etiologic diagnosis may be made from materials obtained for pathologic and bacteriologic studies The prognosis depends on the etiology.

Syphilis of the Trachea, Bronchi and Lungs. Congenital Syphilis. This disease may occur in the larynx, trachea, bronchi and lungs of the fetus and the newborn child Since the tracheal lesions may be the commoner, and all of these structures may be synchronously affected, they are all considered at this time.

Acquired Syphilis. Syphilis attacks any part of the larynx, the vocal cords, the trachea and the bronchi Mucous patches may appear in the larynx Tertiary laryngeal lesions are rare However, they have been reported to result in partial or complete stenosis of the larynx Deep ulcers sometimes occur, and the disease may extend so as to result in external fistulas

SYMPTOMS. Often there are hoarseness and difficult breathing when edema becomes severe Loss of voice may occur in severe infections Laryngeal scarring sometimes results in permanent difficulty in breathing

DIAGNOSIS When the disease is diagnosed by the history, positive serologic reactions, the appearance of the lesions, and biopsy, and if the patient is treated promptly before much destruction has occurred, the prognosis is good There may remain unfortunate conditions such as stenosis of the larynx

Syphilis of the Trachea and Bronchi. Erythema, mucous patches, gummas, perichondritis and subsequent cicatricial stenoses occur in the trachea and bronchi Diffuse gummatous infiltrations are commoner than the localized gumma. They are most frequent at the lower end of the trachea, near its bifurcation; next in frequency come extensions from the larynx, and, lastly, those situated midway between these points. Syphilitic ulceration and stenosis may extend into the main bronchi Complications occur from perforation of the esophagus, aorta, pulmonary artery or vena cava, but the commonest sequela is stenosis.

Syphilitic ulcerations of the trachea are considered to be of rare occurrence Syphilitic stenosis of the main bronchi, without a similar condition in the trachea, is

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In the larynx amyloid deposition is almost entirely associated with a generalized amyloidosis. Though laryngeal symptoms occur, these usually can be detected and identified as a part of the generalized lardaceous process. The lesion occurs more frequently in men than in women in about the ratio of 3 to 1.

The majority of patients are between the ages of 50 and 70 years at the time the diagnosis of amyloid tumor is made In cases reported in the literature, the youngest patient was 19 years of age and the oldest patient was 80 years old.

SYMPTOMS. When symptoms are present, they are caused by the physical presence, size and location of the tumor. There are hoarseness and dyspnea. Willmann reported a case in which the diagnosis was made 6 weeks after the onset of symptoms Thompson described a case in which the chief symptom of hoarseness, in a woman 32 years old, had been present at least 25 years before the diagnosis of deposition of amyloid was made The usual duration of symptoms before diagnosis has been between 1 year and 2 years.

EXAMINATION The gross appearance of the amyloid tumor has been said to be a waxy, translucent, yellow or yellow-gray swelling without ulceration of the overlying mucosa The lesion has been reported to have either a smooth or a nodular outline, and to be either diffuse or well localized and red The tumor is hard on palpation

DIAGNOSIS The diagnosis of an amyloid tumor is determined by microscopic examination of sections of tissue from the lesion. The extent of the lesion may be determined visually by laryngeal examination, roentgenologic examination, tracheoscopy or bronchoscopy Evaluation of the extent of a recurrent lesion or a lesion of which the diagnosis has been established may be simplified by staining of the amyloid by the intravenous injection of Congo red

Malignant Tumors. Malignant disease of the trachea is not common. Most of the malignant growths present in the trachea are but extensions from the larynx, esophagus, or mediastinum. They are much commoner toward the upper end of the trachea than toward the lower end, and more often affect the posterior wall than the anterior wall

The early effects of malignant neoplasms are similar to those of innocent growths in the air passages, namely, dyspnea, cough, and expectoration with hemoptysis

In regard to frequency of hemoptysis in nontubercular disease of the trachea and lungs Jackson and Diamond found the principal causes to occur in the following order of enumeration. bronchiectasis, primary bronchial carcinoma, tracheobronchitis, pulmonary abscess, no evident disease, nonsuppurative pneumonitis, suppurative pneumonitis, bronchial adenomas, secondary pulmonary cancer, primary tracheal carcinoma The manifestations of a pulmonary abscess may be produced, with severe toxemia An extensive growth produces cachexia, pain if spreading into the mediastinum, and dysphagia if involving the esophagus

The physical and roentgenologic examination will reveal the situation of the tumor in most cases, but it is generally necessary to make a bronchoscopic examination, which also affords an opportunity for biopsy

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The thin ones of postures 3 and 4 (Fig. 6-1) suffer with the functional disturbances known to affect the visceroptotic type Those who have postures like those of 3 and 4 (Fig. 6-2) are hypersensitive about both their posture and their degree of obesity.

In many families it seems that posture is heritable.

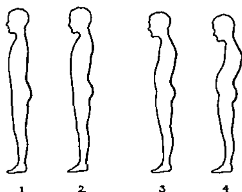


Fig 6-1 Postures of persons of normal or less than normal body weight Posture 1 is excellent, 2 fair, 3 poor, and 4 bad

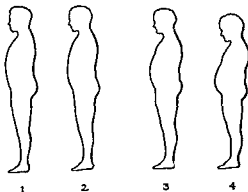


Fig 6-2. Postures of the obese. Posture 1 is excellent, 2 fair, 3 poor, and 4 bad.

Dynamic Posture. Dynamic posture is posture in motion or in action or in preparation for action It includes the transitions between the static positions of lying, sitting and standing and also such activities as pushing, lifting, walking, running, climbing, jumping, dancing, swimming, work and play. Dynamic posture includes the uses of the upper extremities and the trunk as well as of the legs, and the relationships between the various parts of the body in action Dynamic posture includes locomotion, which requires the combined use of all four extremities Poor dynamic postures are characterized by awkwardness and inability of performance and are present in diseases of the central nervous system.

The basic dynamic posture is characterized by a slight crouch, with the ankles, knees and hips flexed, the head and trunk inclined forward and the trunk slightly flexed, the arms relaxed and slightly flexed. With the body in this position the muscles are in a midposition with increased tone, balanced and ready for instant and powerful action in any direction They act also as springs, absorbing shocks and initiating movement

Walking. Walking may serve as an example of dynamic posture. The body is tilted slightly forward from the basic standing position and the weight is thrown on the ball of the foot, while the other thigh is lifted and the leg and opposite arm are swung forward Various muscles, aided by inertia, maintain the body in balance on the ball of one foot until the opposite heel strikes, when the weight quickly advances to this leg with the knee extended Momentum carries the body forward over the extended leg until it passes the perpendicular, when the thrust of the foot renews the action and the process is repeated with the opposite foot and leg (Fig 6-3)

Correct walking is done with a smooth rhythm, the muscles contracting gently with a brief wavelike action and relaxing in the interval. It is characterized by free muscle and joint action, momentum, balance and rhythm Effort becomes much greater if the speed is increased or if momentum and rhythm are disturbed

Alertness, nimbleness, speed, smoothness and steadiness are required for the development of dexterity Dexterity is the requisite for the synchronization of the movements necessary for the performance of proficient and deft walking, especially at a military cadence of 120 steps per minute These attributes are obtained by (1) a heritage of good muscles and (2) a lifetime of careful training and control

6

DISEASES AFFECTING LOCOMOTION

Diseases affecting locomotion interfere with the modes of the body such as posture, gait, equilibrium and often positions while in bed, at rest and during illnesses These modal disturbances result from and are the manifestations of diseases of the skeleton, the peripheral vascular circulation, muscles and nerves

POSTURE

The term posture refers to the sum total of the positions and movements of the body. Static posture refers to the different positions of rest and the variations of these positions Dynamic posture refers to the body in motion or in action It is by means of these postures that the body attains comfort, mechanical efficiency and physiologic function while at rest and during locomotion. Disturbances in posture are frequent accompaniments of diseases affecting locomotion.

Static Posture. Static posture is the posture while at rest. It includes the normal positions for lying, sitting and standing *Lying* is more easily assumed than any other position Static posture may be affected by diseases of the skeletal structures and also by diseases of the heart and lungs.

Sitting. The usual sitting position is with the trunk and head erect and centered over the pelvis or tilted slightly forward, with a medium or slight lumbar arch and with the hips and knees flexed at a right angle The sitting posture may be the only comfortable posture available to those who have congestive heart failure.

Standing. In the standing position the body is vertical and essentially straight when seen from the side as well as from the back. The position is maintained with the spinal column rather than the shoulders The body achieves its full height in this position, with the head and chin level, not tilted back The weight is slightly more on the heels than on the toes, although in the dynamic position of expected forward movement the weight shifts toward the toes. A strong man or woman may faint if required to stand rigidly for a long time (30 minutes or more) because of the relatively static condition of the circulation and the accumulation of blood in the vessels of the lower extremities Ankylosis of both hip joints in extension limits the postures to those of standing and lying

The length of time that a person can stand without fatigue is related, among other factors, to the posture A person of good posture as represented by postures 1 or 2 (Fig. 6-1) can stand much longer without fatigue than a person of poor posture. Postures 3 and 4 (Fig 6-1) represent those of persons who have poor muscle tone from lack of exercise or from disease.

Obesity changes the postural appearance. Those who have good postures such as *postures 1 and* 2 (Fig 6-2) may not be handicapped while they are young However, as age advances, postures 3 and 4 (Fig 6-2) are assumed.

Postures 3 and 4 (Figs 6-1 and 6-2) will not permit proper space for good physiologic functioning of the organs of respiration and digestion Posture is always an important diagnostic consideration in diseases of the heart and lungs.

During youth, if the person is otherwise healthy, poor posture may not be measurably detrimental to the state of health. However, as the years advance, those of poor posture are noticeably more prone to poor health than persons of good posture

shoes, corns, rheumatism, gout, sciatica, metatarsal neuralgia, hip-joint or knee-joint disease or injury (recent or old), sacro-iliac disease, sprains, inflammatory disease of the extremities, short leg and paralysis of one leg, give rise to a limping or hobbling gait. The most characteristic methods of abnormal progression are seen in diseases of the nervous system.

Ataxic Gait. In walking, the foot is raised suddenly and too high, the leg is thrown forward with unnecessary vehemence, and the foot is again brought to the ground heel first, or flat-footed with a stamp The feet are usually planted wide apart, and while they are in the air they move as if the patient were doubtful where to put them. The body is bent forward, and the eyes are fixed on the ground in order to supplement as far as possible the loss of muscular and articular sensation. This gait is extremely characteristic of locomotor ataxia

Cerebellar Ataxic Gait. The manner of progression resembles that of an intoxicated person The patient walks with short steps and with his feet wide apart, staggers, reels, sways to and fro, and reaches a set point by zigzagging toward it. The swaying is relieved if he is supported by the hands of the observer placed under the armpits This gait is significant of a tumor of the vermis or middle lobe of the cerebellum, and is often called the titubating gait, or simply cerebellar ataxia A somewhat similar gait is seen in Friedreich's disease, hereditary cerebellar ataxia, dementia paralytica, ataxic paraplegia, labyrinthine disease and, to some extent, vertigo from any cause.

Steppage Gait. This variety of gait is due to paralysis of the extensor muscles of the foot whereby, when the foot is lifted, its anterior part tends to hang or drop down. In order to prevent the toes catching and tripping against the ground, the leg carries the foot somewhat forcibly forward, raising it at the same time unusually high, thus throwing the toes upward and bringing the foot to the ground heel first Steppage gait resembles the gait of a man who is walking through snow, thick grass or brushwood It is evidence of peripheral neuritis of the anterior tibial nerve, and because of a certain resemblance to the gait of locomotor ataxia, is sometimes termed the pseudotabetic gait

Spastic Gait. The legs are rigid and move stiffly, and there is apparent difficulty in bending the knees In consequence the foot is dragged along, the toes catching and scraping on the ground In some instances, owing to spasm of the adductors of the thigh, the legs and knees touch and cannot be separated, causing cross-legged progression, that is, the legs and feet overlap at each step This gait depends on the excessive tension and spasticity of the muscles arising from lesions of the upper motor neurons. It is therefore, when bilateral, significant of sclerosis affecting the lateral pyramidal columns of the cord. The mode of walking in hemiplegia is a unilateral form of the same gait The paralyzed leg, by a tilting of the pelvis, is swung outward and around to the front, the toes often scraping the ground

Festination. The head and body are bent forward and the patient takes short, shuffling, hurried steps, his speed tending to increase as he progresses, exactly as if he were being constantly pushed forward and were trying to prevent it. This gait is termed festination or propulsion In some instances, if the patient is pulled rather suddenly backward, he will take a number of backward steps (retropulsion), although the body remains in its forward-leaning attitude This gait is characteristic of Parkinson's disease and extrapyramidal neuron disease

Waddling Gait. The shoulders are thrown back, the back is hollowed (lordosis), and the abdomen protuberant, the body sometimes actually leaning backward In walking, the feet are planted wide apart and the body swings from side to side at each step—the waddling or duck gait. It is a very characteristic symptom of pseudohypertrophic muscular paralysis. It is seen also in disease, or congenital dislocation, of both hip joints

over the motive parts involved in dynamic posture. A lack of these attributes may indicate disease

Walking with a limp may result from pain, weakness, stiffness or deformity. Pain may be caused by an injury, such as a sprain, fracture or bruise, a blister, a corn, or an inflammation such as arthritis. Weakness may be due to many things, such as lack of sleep, improper diet, illness, heat and humidity, a poor heart, lung disease or nerve or muscle damage Stiffness may be due to muscle or joint damage, or to tense or contracted muscles. Deformities such as knock knees, bowlegs, short or twisted

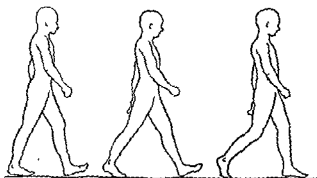


Fig 6-3 Walking Taking one step forward.

legs, clubfeet and high or relaxed arches have their individual effects on manner of walking.

The security of balance and ease of walking or running are enhanced by swinging the opposite arm and leg forward and backward with each step as if in four-footed locomotion. The normal co-ordination of movements of the extremities may be either exaggerated or lost when there is a limp.

Poor Posture. Poor posture may be due to changes in muscle tone or to changes in skeletal structures Irrespective of the cause, a poor sitting posture is characterized by a drooping of the spinal column and trunk, with the lumbar and thoracic portions of the spinal column flexed, the pelvis tilted back, the abdomen and chest flattened and compressed, and the shoulders and head forward A poor standing posture is characterized by a forward movement and tilt of the pelvis, with an increased lumbar lordosis and an increased thoracic kyphosis In this poor standing posture the knees flex, the abdomen sags and protrudes, the chest flattens, and the shoulders, head and neck are advanced. The height is diminished, and the body as seen from the side forms a long S curve.

Muscular Tone. The tone of the muscles has a great deal to do with posture. *There is the large group of persons who have hypotonic muscles and elongated* ligaments with joints which extend too far These hypotonic persons may have weak arches, knock knees, bowlegs, torsion, wryneck, stooped backs, curvatures of the *spinal column, and weak lumbosacral joints, any one or a* combination of which affects posture Any disease or injury which causes tonus changes in the muscles, ligaments or bones is often the cause of poor posture In addition, poor posture may *result from poor training or poor habits*

Gait. The manner of walking is closely associated with the manner of standing. In order to observe the mode of walking, the examining physician requests the patient to walk away *from and back to him, to walk at right* angles to the line of sight, and to walk along a crack between the floor boards or a seam of the carpet.

In pregnancy, ascites, large abdominal tumors, cretinism, pseudohypertrophic [illegible] widely separated so

[illegible]

Painful or [illegible] [illegible] mities, such as tight

fevers, such as typhoid fever, even at an early period, because of the marked muscular weakness and mental apathy so characteristic of typhoid fever. It may be present in motor apathy, which often attends frontal lobe brain tumors.

RIGID DORSAL POSITION IN BED A rigid dorsal position, with both legs drawn up, in order to diminish abdominal tension, is the rule in general peritonitis and in many cases of pelvic peritonitis In appendical peritonitis the right leg alone may be flexed In hip disease also there is flexion of one knee

ON SIDE IN BED. The patient may lie on the side, and the manner of lying may be active or passive, as in the dorsal position There are many persons who cannot rest on one or the other side because of discomfort or actual pain. Often no assignable reason can be found to account for this manifestation of discomfort.

Patients having acute one-sided affections of the thorax usually lie on the affected side to limit its movements and lessen the pain caused by pleural friction, as well as to afford greater freedom of compensatory motion to the healthy side. Moreover, if a large pleural effusion exists, the pressure due to its weight will not burden the heart and the healthy, uncompressed lung when the patient lies on the affected side The posture of a patient with a cavity in the lung is of some significance, that position being chosen which brings the opening of the cavity uppermost, thus allowing secretions to accumulate and be discharged at infrequent intervals instead of constantly trickling into the bronchial tubes and causing an incessant irritating cough. The rule of lateral decubitus is not invariable, since the patient may find other positions preferable In sciatica the subject usually lies on the unaffected side

The lateral position, with the legs drawn up to meet the trunk (the coiled posture), is seen in meningeal, cerebral and cerebellar disease (due to spasm), and in hepatic, renal and intestinal colic

OPISTHOTONOS. Opisthotonos is an uncommon dorsal position in which the body rests on the head and heels, the trunk being arched upward. It is observed in strychnine poisoning, tetanus and uremia, as well as in some peculiar manifestations of hysteria A modification of this position is observed in the characteristic contraction of the posterior neck muscles in meningitis, whereby the back of the head bores into the pillow

EMPROSTHOTONOS Emprosthotonos is an attitude in which the upcurved body rests face downward on the forehead and feet It is the opposite of opisthotonos and is rarely seen, but may be observed in tetanus, strychnine poisoning, paralysis agitans and cerebrospinal meningitis.

THE SKELETON

The diverse activities to which mankind is adaptable are first of all dependent on skeletal design The skeleton is composed of the axial and the appendicular divisions The axial skeleton is, as the name suggests, the center or the axis about which the movements of the appendicular skeleton are resolved.

The *axial skeleton* embraces the bones of the head, the spinal column and ribs, the hyoid bone and the breast bone The spinal column includes the vertebrae of the cervical, thoracic and lumbar regions, and the sacrum and coccyx.

The *appendicular skeleton* embraces the bones of the extremities, including the shoulder girdle or thoracic girdle, formed by the scapula and clavicle, to which the upper extremities are attached, and the pelvic girdle, formed by the innominate bone, to which the lower extremities are attached.

In the four-footed position the appendicular skeleton is concerned only in locomotion In the upright position assumed by man, locomotion is more complex. The upper extremity is freed from its main function of locomotion to follow the will of the brain In order to subserve the hand in the performance of its diverse functions, the back, a part of the axial skeleton, has assumed more elasticity in order that it may bend to carry the hand to its appointed tasks.

Equilibrium. Equilibrium is a state of balance or equipoise; a condition in which opposing forces exactly counteract each other. Clinical histories of those who have sustained injury from sudden loss of lateral equilibrium are common. Lateral equilibrium is often lost while one is carrying a weight in one hand. However, injury to the back may be sustained without a loss of lateral equilibrium if a heavy weight is carried in one hand and the pace is hurried or lengthened.

Lateral equilibrium can be disturbed by a deviation of the spinal column above the sacrum and to one side and also by anything that affects the length of either leg When a position of rest is desired, the hips are moved laterally so that the center of weight falls on one leg, which is kept extended The opposite hip then descends until further adduction is stopped by the superior ligaments of that hip

In order to maintain balance, the movements of the body must be properly performed and a relationship of the parts one to the other must be maintained. This must be true whether the body is in a state of motion or of rest. During motion the muscles control the position of the bones. During rest the position of the bones is controlled by the ligaments. The weight of the body acts as a constant force pressing downward, and it is nicely balanced on the bones by the ligaments, aided by the muscles. A weakness of any one of these three elements, ligaments, muscles and bones, may permit balance to be altered.

If balance is altered, deformity ultimately will result. Distortion of a bone as the result of a badly united fracture throws the weight and muscular action too much to one side, with the result, first, that action of the part is impaired and, second, if use of the part is persisted in, deformity results and increases. If there are relaxation and weakness of ligaments during adolescence and if the ligaments give way in the foot, for instance, flatfoot results, in the knees, knock knee results, and if in the back, scoliosis or lateral curvature If the muscles give way, as in poliomyelitis, deformities result which may have to be corrected, if they can be rectified at all, by the proper application of braces or by tendon transplants.

Mode of Moving. In certain ailments there is unusual *immobility* due to the increase of pain on motion, as in arthritis, scurvy and rachitis, or a disinclination to move because dyspnea is made worse by exertion. Paralysis or tonic spasm of large muscular groups is another cause of enforced quietude

An opposite condition, *restlessness*, exists in many diseases, as in fevers, large hemorrhages and hyperthyroidism. Agitated and irregular movements are seen in chorea, in hysteria, with its manifold manifestations, and in other diseases of the nervous system Severe griping or colicky pain, gallstone colic or renal colic will induce the patient to throw himself about in the hope of relieving his suffering

Posture in Bed. Rest in Bed. The patient usually takes to bed in acute illness or in chronic ailments because of general weakness, pain, or inability to remain up and around In some cases the patients may assume that they are unable to be up, though they do not have pain, weakness or fever. In some special cases there is interference with the use of the limbs, as in certain diseases of the nervous system.

Many persons in health habitually assume certain attitudes while in bed, and their customs in this respect may not be changed by illness. Because of this fact the postures assumed in disease and their diagnostic associations are described as follows:

Static Posture in Bed. In the dorsal strong or active posture the patient lies on the back comfortably and without constraint. This posture is seen in health and in slight illness unattended with great pain

Passive Posture in Bed. In the dorsal inert or passive posture the patient lies on the back but is constantly slipping toward the foot of the bed, thereby putting the body in a posture which is uncomfortable and which interferes with the respiratory movements. The passive posture is observed in conditions of great weakness, most frequently in the acute infectious diseases. It is especially characteristic of severe

fibrous tissue. The disks are attached to the cartilaginous plates of the vertebral bodies and are pulpified centrally to cushion the vertebral column, for instance on jumping and landing suddenly on the feet.

The skeletal muscles control the motion of the back within the limits determined by the ligaments These muscles are arranged in symmetrically opposing groups Posteriorly the short and long intervertebral muscles attached to posterior and lateral processes, the vertebrocostal, vertebro-iliac and vertebrosacral groups are extensors of the back and acting in unison with other groups, rotation and lateral bending are accomplished

The tissues of the back are innervated and nourished by the posterior divisions of the segmental nerves and blood vessels.

Variations and Anomalies of the Vertebrae. Each human vertebra is formed by the fusion of adjacent halves of two primitive somites and passes through membranous and cartilaginous stages to become bone

Irregular fusion of the half somites gives rise to hemivertebrae, a frequent anomaly When it occurs, there is usually a corresponding anomaly on the opposite side of the column a few segments distally which corrects the order of fusion. Though the lesion causes deformity of the back, it is of no great clinical importance

In the human vertebral column the number of segments of the vestigial coccyx and of that part of the sacrum distal to the articulations with the ilia is of no particular consequence. The number of cervical segments is found to be remarkably constant The thoracic vertebrae, distinguished by attachment of ribs, vary in number from 11 to 13, the modal number being 12 The number of lumbar segments varies from 4 to 6 from a mode of 5 There is frequently a gain or loss of one thoracic segment with compensatory loss or gain of a lumbar segment, the total number of presacral segments remaining unchanged Evolutionists aver that in man there has been a progressive shortening of the presacral column which has been synchronous with specialization in skull, brain and teeth

The first sacral segment of the vertebral column is determined by the level at which the ilia articulate with the column to form the sacro-iliac joints These are formed by the approach of the ilia, developing in the limb buds, to conjugate with the vertebrae The meeting is usually, but not always, bilaterally symmetric Lagging of one ilium behind the other results in asymmetric sacralization of the last lumbar or first sacral segment

The partial loss or gain of a segment, as in the case of unilateral or bilateral sacralization of the last free segment with large transverse processes impinging on or articulating with the sacrum or ilium, narrowing of the lumbosacral disk or formation of a false promontory, rarely causes disability

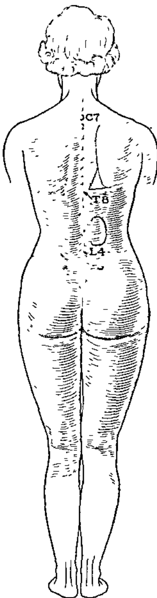


Fig 6 4 Topography of the back C7, seventh cervical vertebra, T8, eighth thoracic vertebra, L4, fourth lumbar vertebra

Defects in closure of the neural canal and in development of the articular processes which anchor the lumbar column to the sacrum may occur In such instances the supporting structures of the sacrum may lie in any position between the sagittal plane characteristic of the lumbar vertebrae and the transverse plane of the sacrum, and frequently these defects vary bilaterally and may definitely affect the stability of the lumbrosacral anchorage. It often predisposes to a forward displacement of the involved vertebra on the segment below. This forward displacement is known as spondylolisthesis.

Skeletal Anomalies. Anomalies of the axial skeleton comprise, first of all, those of the head. These anomalies are great and mainly are incompatible with life. Individuals who survive with head anomalies often have mental derangements (see Complaint, Chapter 2; and Chapter 4). The rest of the anomalies of the axial skeleton are for the most part related to the number and development of the vertebrae and thus will be mentioned in relation to the vertebrae

Anomalies of the appendicular skeleton are related to the extremities. The limbs either may fail to develop at all or may be present as mere rudiments of structure (amelus). Sometimes the proximal segments of an extremity are normal while the distal portion is deficient and tapers to a stump (hemimelus). In the reverse conditon at least the proximal segment is missing and the hand or foot springs directly from the trunk (phocomelus) Union of the legs produces the mermaid condition (sympodia). A number of deformities may be associated when the hands or feet lack digits, for example, split, or cleft, anomaly of the hand and comparable deformities of the feet. Opposite in nature is a partial or complete duplication (dichirus). An example of dichirus is *polydactylism*, which usually is characterized by the addition of but a single digit The bony fusion or fleshy webbing of digits (*syndactylism*) is usually limited to union of the middle and third digits. Abnormal shortness of the digits is *brachydactylia*, due either to the omission of phalanges or to digital shortening The opposite tendency is hyperphalangism, in which supernumerary phalanges are interpolated in the customary digital series. All of these malformations of hands and feet tend to be strongly heritable (Arey).

Clubhand or *clubfoot* may result from primary defects in the differentiating limb buds with malformed muscles.

Congenital elevation of the shoulder results from an arrested descent of the upper limb from its cervical, embryonic position. Congenital dislocation at the hip joint results from failure of the outgrowths that normally produce a brim about the socket floor of the joint *Intra-uterine amputations* (at any level) are due to focal deterioration and not to constrictions by loops of the umbilical cord or amniotic bands (Arey).

THE AXIAL SKELETON AND LOCOMOTION

The Back and Spinal Column. On inspection of the back of a normal person who is undressed and standing erect, a median depression is observed to commence at the lower part of the line of the scalp and to extend almost straight down the back to the sacrum (Fig. 6-4) The prominence of the seventh cervical vertebra and the first thoracic vertebra can be seen. In the middle of the depression the spaced elevations representing the spinous processes of the vertebrae often can be seen and always can be palpated They form an approximately straight line. These prominences end at the beginning of the sacrum

From the superior border of the sacrum, down to near the top of the gluteal folds, is a triangular space with its base above and apex downward. The apex of this triangular space marks the third sacral vertebra. Laterally opposite the second sacral vertebra the posterior superior iliac spine is palpable The elevations limiting the apex of the triangle are formed by the erector spinae muscles.

Laterally from the furrow, in the thoracic region, the projections of the scapulae are visible. If the arms are by the sides, the borders of the scapulae are parallel to the median line. The inferior angle of the scapula is opposite the upper border of the eighth rib The medial angle covers the second rib but its tip is level with the first rib. The twelfth rib usually projects to just beyond the outer edge of the erector spinae muscle. The outer edge of this muscle is marked by a depression separating it from the abdominal muscles in front

On the inner side of the lower third of the posterior edge of the scapula is a small triangle. The upper side of this triangle is formed by the trapezius, its lower side by the latissimus dorsi, and its lateral side by the posterior edge of the scapula. As the lung is nearest the surface at this point, this triangle is often chosen for puncture

The spinal column is composed of a complex arrangement of bones, joints, muscles and fasciae. Between each two of the presacral vertebral bodies is a disk of specialized

poliomyelitis. It is often the result of the contraction of one lung after pleurisy or empyema.

The development of scoliosis shifts the center of gravity from the midline to one side so that it falls nearer to the foot on the side toward which the trunk is inclined than to the contralateral foot (Fig. 6-4). To compensate for this shift of weight, the hips are inclined to the opposite side, and the center of weight is brought by this inclination once more midway between the ankles. However, if the single curve of scoliosis is complete and again reaches the median line, as is usually the case in scoliosis, the center of weight may not be disturbed; and if not, lateral shifting of the pelvis does not occur There are instances in which the curves are so irregular that more of the weight shifts to one side than the other; when this takes place, the pelvis shifts, and the hip on the side opposite to the inclination appears to be higher than the other (Fig. 6-5).

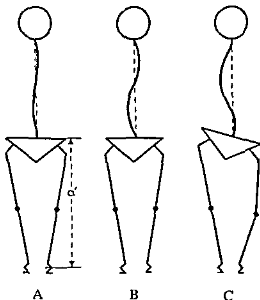


Fig 6-5 Deviations of the spinal column above the pelvis and measurements of the length of the legs

The line joining the two anterior superior iliac spines should be at a right angle with the long axis of the body, as in A and B, before measurements are made

If a hip is ankylosed, its femur is moved laterally, by the examiner, until the line joining the anterior superior spines is at a right angle to the body The opposite femur is made to correspond in position before measurements are made

The line a' (the distance from the anterior superior spine of the ilium to the tip of the internal malleolus of the tibia) when the foregoing conditions have been met gives the length of the leg in question This is compared with the same measurement of the opposite leg

Legs of unequal length cause the pelvis to tilt down on the side of the short leg as in C

Measurement of the Lower Extremities. Under ordinary circumstances, in the absence of deformity or limping, the lower limbs are assumed to be of equal length When on measurement one can detect difference in length of the legs (1 inch or more), there usually is enough deformity to produce unevenness of the gait, for instance a limp (Fig 6-5)

If the legs are of unequal length, the pelvis tilts to the side of the shorter limb, carrying the lower part of the spinal column with it and producing a convex curve, again on the side of the short leg, which is not marked in the lumbar region. The middle and upper parts of the spinal column are carried to the opposite side of the convex curve In patients thus variously affected, the deformities may be great In some the spinal curvature may extend as high as the shoulders and in these the hips may be observed to be uneven in height. The unevenness in the length of the legs may be such that the unequal length is obvious and the gait is markedly limping

Backache and Pain in the Back Without Sciatic Radiation. There is more good evidence to indicate that backache can be definitely associated with misuse and abuse of the back than there is that it results from an upright posture and plantigrade gait. However, it is recognized that the anatomic rearrangements required to change from a pronograde animal to one with an upright posture and a plantigrade gait were extensive From evolutionists (Sir Arthur Keith) we learn that these

More difficult to recognize is spina bifida occulta, in which there is no external mass. The patient may have no complaints or may complain of slight motor, sensory or trophic disturbances in the lower extremities. Over the lower part of the back in the middle line there may be an area of hypertrichosis. On palpation a defect of the vertebral spinous processes in this region may be made out.

At the lower end of the sacrum there is sometimes an abortive tail. This may be a true tail, containing rudimentary vertebrae, sometimes the appendage does not contain bone.

It is generally felt that complete sacralization of the last lumbar vertebra is not a cause of pain, but that partial sacralization of this vertebra produces pain through irritative changes occurring at the site of the false joint. These irritative changes may occur solely in the soft tissues, or eventually they may cause osteoarthritic changes to take place at the site of pseudoarthrosis

Curvatures of the Spinal Column. At birth there are a thoracic and a sacral curve of the spinal column Both of these are convex posteriorly Laterally there is a slight curve in the thoracic region with its convexity to the right or the left, depending on the handedness of the individual

If the height of the two shoulders in the adult is unequal, the lower shoulder usually indicates the handedness; usually the right shoulder is the lower in right-handed individuals A marked difference in height of shoulders increases the chances that a rotary scoliosis is present

The symmetric, or anteroposterior, curvatures of the spinal column are kyphosis, convexity backward, and lordosis, convexity forward An asymmetric or lateral curvature is scoliosis As a rule there are moderate kyphosis of the thoracic region and moderate lordosis of the lumbar region Practically, the lateral curvatures, or scolioses, are the most important of the abnormal curvatures

Curvatures of the spinal column may result from faulty development or may arise from diseases of the spinal column itself. Faults of skeletal development such as supernumerary ribs or absence of a rib may cause scoliosis Spondylitis is often a cause of kyphosis or of scoliosis. Curvatures may develop in the course of Paget's disease, acromegaly or syringomyelia. Ordinarily curvatures of the spinal column depend on softening of the bones of the spinal column due to rickets, early or late, or to osteomalacia

Kyphosis, especially in the thoracic region, is seen in many elderly persons It forms part of the changes which constitute an emphysematous thorax. A kyphotic condition may be present also in rachitic children and in young persons who are weakened by acute or long-continued illness These posterior curvatures are to be distinguished from the more or less sharply angled kyphosis of Pott's disease. In some patients, children in particular, there is a somewhat unusual but normal prominence of the seventh cervical vertebra or the eighth and ninth thoracic spinous processes

Lordosis occurs usually in the lumbar region and is an exaggeration of the normal [illegible] ascites, and [illegible] strophy. [illegible] sociated with orthostatic albuminuria

Scoliosis is a rotary lateral curvature of the spinal column, with prominence of one scapula. If one scapula projects, it indicates the existence of lateral curvature and the existing causative conditions, or paralysis of the serrator anterior muscle on that side. If both scapulae are abnormally projecting, it is probable that the patient has an alar or a pterygoid thorax.

Scoliosis may indicate unequal length of the lower extremities; the habit of standing habitually on one leg or carrying weights on one side; muscular weakness from fever or anemia, or general debility, congenital or acquired. It may also result from the tilting of the pelvis in old sciatica, and from paralysis due to anterior

shows great limitation of back motion. Spasm is present, and percussion reveals localized pain and tenderness over the affected vertebra or vertebrae.

Early in the course of the disease the diagnosis is difficult to make on the basis of the roentgenographic findings; later it is somewhat more easily made. The shadow of paravertebral abscess may indicate an infectious lesion. In general, granulomatous lesions such as tuberculosis cause destruction of bone and cartilage, and the bone has little or no tendency to heal until late in the course of the disease. Active pyogenic infections cause early destruction of bone. Proliferative bone healing occurs readily and there is little actual decrease in the width of the vertebra or interspace.

The differential diagnosis of the infectious organism causing destruction is difficult when there is no history of a preceding disease. Blood cultures may help in the [illegible] tion of the abscess and subsequent bacterial culture and animal inoculation will establish the etiologic diagnosis.

Trauma. In any injury to the spinal column or its structures which has not injured nerves or the spinal cord, the patient walks carefully without jarring. This caution is greatly increased if the sacro-iliac joints have been injured.

In severe soreness of a sacro-iliac joint the gait is suggestive The patient carefully avoids putting weight on the affected side of the pelvis, either while walking or while sitting In the sitting position the weight of the body is maintained on the opposite ischial tuberosity

Strain. Back strain indicates an applied stress greater than that which the supporting elements are normally able to withstand. If the tissues of the back are abnormal at the time of injury, there may be an invasion by an inflammatory process and convalescence may be delayed Soreness, stiffness and weakness persist longer than the seriousness of the injury would justify.

In acute traumatic back strain there is localized tenderness with muscle spasm and pain. The posture will be that of giving way to the injured side in order that tension may be relaxed on the affected side The pain may extend down the back of the hip and thigh, or around to the inguinal region

In back strain the findings of roentgenographic examination are negative.

Flat Back Strain. Flat back strain occurs in the pyknic type of body (Fig. 6-2, posture 4) The strain develops in the lumbosacral region, with lordosis absent in the sitting, standing and supine positions, and with all activities limited by pain which is relieved only when the patient lies supine with the legs outstretched. Stooping forward in the sitting position may be free, but recovery in the upright position is labored and hyperextension is impossible because of pain. The side-lying and the prone positions are uncomfortable The roentgenogram reveals an unusually vertical sacrum

Sprain. The term sprain is applied to a joint that has been suddenly twisted or wrenched, thereby stretching the ligaments until they become torn or separated from their attachments Severe sprains are much rarer than are strains.

After a back sprain there is immediate disability and the symptoms are more severe than in case of strain There may be severe suffering accompanied with nausea and faintness In severe sprain there is muscle rigidity and there is a definitely localized region of deep sensitiveness and tenderness There may be noticeable swelling over the region of the damaged tissues.

A sprain of the back may be expected to heal as quickly as sprained ligaments of other joints, but a residual soreness due to fibrous hyperplasia and often adhesions or scar tissue may prevent work for several weeks after the primary healing has

changes have imparted structural weaknesses. These structural weaknesses, which seem to have commenced in the caudal end of the spinal column, involve most of the muscles and the corresponding nerve centers which control them. In contrast to the weaknesses is the formation of the sacrum, which serves to shorten and strengthen the spinal column

The whole weight of the suprasacral part of the human body is supported erect on the spinal column over long periods of time. The demands on the neuromuscular postural mechanism are even greater in the sitting position than in the standing posture, particularly if the individual sits leaning forward, as in writing or reading The muscles which act on the short levers of the spinal column yield first, while the muscles which act on the long costal levers can still keep on The human being rests these exhausted short spinal muscles by allowing the vertebrae to rotate until the articular processes begin to lock and the transverse processes rest on the neck of the long costal lever Therefore it is more restful, at least for short periods of time, to sit somewhat slumped forward It is an erroneous idea that sitting practically upright is less exhausting.

Backache in the lumbar region, or lumbago, is a common discomfort in those who are acutely or chronically ill and in those who have overworked Backache may be due to causes within the confines of the spinal column, or it may be due to causes situated within the supporting structures of the spinal column. And, finally, it may result from disease of the viscera in the thoracic, abdominal or pelvic regions

Backache is not a disease, only a symptom that may be due to any one of different causes

Postural Backache. The position assumed in poor posture of advanced degrees is familiar to all. The head protrudes, the shoulders are rounded and dropped, the chest is flat, and the thoracic portion of the spinal column has an increased posterior convexity or kyphosis. The lumbar lordosis is exaggerated and the abdomen is protuberant, particularly in its lower half The pelvic inclination is increased Some persons have a flattened lumbar lordosis and compensation takes place by flexion of the hips The knees are slightly flexed and the feet are pronated All degrees of these postural aberrations are encountered

Many people habitually assume, at work or at other times, positions of great mechanical instability, and sooner or later, under the stress and strain, backache results

One common cause of chronic strain in the lower portion of the back is a sagging or protuberant abdomen (Fig 6-2) which, by its weight and its downward and forward pull, tires the muscles and leads to increased tension on the ligaments supporting the lumbar portion of the spinal column. The postural backache of pregnancy is explained on the same basis

The tall, slender individuals with poor posture hyperextend the lumbar regions of the spinal columns. The long, slender type of back is unable to withstand an increased strain for any length of time (Fig 6-1).

Alteration in Plane of Facets. The frequency with which alteration of the plane of articular facets of the lumbar portion of the spinal column occurs is not known. When in the three-quarter roentgenographic view of the spinal column, the facet or facets are found to be placed in a plane that is different from that of the other lumbar facets, the joint cannot move in unison with the remaining joints of the lumbar part of the spinal column; and thus function is impaired and irritative [illegible] of the anomalous articulation may produce pain

[illegible] The blood-borne organisms find vertebral bodies [illegible]. The intervertebral disks are relatively avascular [illegible]ly.

Symptomatically, the patient has a backache which is usually sudden in onset, severe and disabling, along with fever and leukocytosis Objectively, the patient

the shaft of the femur; (5) carcinoma of the rectum, or of the prostate, (6) malignant disease of the female genitalia; (7) the pains of tabes, or of dementia paralytica; (8) ruptured intervertebral disk; (9) intermittent claudication, (10) neuritis of diabetic or other metabolic or nutritional causes and (11) metallic poisonings. However, backache with sciatic extension is most frequently associated with arthritic changes of the lumbosacral joints.

Sciatica (*Sciatic Neuralgia*). Sciatica, or neuralgia of the sciatic nerve, is characterized by pain in the distribution of the sciatic nerve. The causes enumerated in the list of diseases and conditions which may cause backache with sciatic pain are many (*vide supra*). Many of these diseases may be difficult to diagnose. It is for these reasons that the diagnosis of sciatica without a cause is not safe to make However, in practice there are a number of patients who will have sciatica from unknown causes, the idiopathic sciaticas

These instances of the so-called sciatic neuritis or ischemic sciatica (idiopathic sciatica) occur more frequently in men between the ages of 30 and 50 years of age than in women, or than in men of other ages The symptoms commence with pain situated mainly in the back of the thigh The pain is dull and almost continuous with paroxysms of sharp pain and burning The nerve is tender on palpation.

There are other neuralgias of the lower extremity, for instance those of the femoral nerve (anterior crural neuralgia), the external cutaneous femoral nerve (meralgia paraesthetica) or the obturator (obturator neuralgia).

Meralgia Paraesthetica. This is a variety of pain localized in the area of the distribution of the external cutaneous nerve on the lateral side of the thigh. The pain is often induced by standing or walking Obese middle-aged men are more commonly affected than are women The presence of an area of impaired sensation indicates a neuritis rather than a neuralgia Bilateral pain has been observed.

Sciatic Scoliosis. Ellis employs the term sciatic scoliosis to designate lateral deformity of the trunk secondary to a painful minor lesion in the lower part of the back, the buttocks or the sciatic nerves The characteristic lateral tilt of the trunk represents a posture which will relieve or mitigate the pain producing the syndrome.

The etiology of sciatic scoliosis is variable and may be difficult to elucidate. When the cause is a lumbosacral pathologic change, there is a rather sharp lateral deviation of the lumbar portion of the spinal column at the lumbosacral junction without any pelvic rotation.

In spinal arthritis and sacro-iliac disease there may be a generalized bending of the lumbar portion of the spinal column without rotation and deviation. If bending of the lumbar vertebrae is great enough, the scoliosis may be compensated for by a slight tip of the pelvis upward on the side toward the convexity, and the leg on the affected side may be flexed at the hip and knee.

A myelogram may be required to eliminate the possible presence of a protruded intervertebral disk

Traumatic Sciatica. Woltman recorded 77 cases of neuritis of the lumbosacral plexus in each of which there was sciatic pain In 11 of these cases the neuritis was due to trauma, such as excessive flexion of the thigh, hyperextension of the thigh during a dive, fracture of the sacrum, football injury, or a fall from a horse

During sleep a postural injury of the nerve may occur When the lower extremities are compressed in some unusual position, as over the edge of a bed-rail, whether the pressure injures the nerve fibers or the nutrient vessels of the nerve trunk is conjectural

Other Forms of Backache. Other, less severe and some less common, types of pain in the back that occur often enough and present enough similarities to justify mentioning are nocturnal backache, the backache that accompanies menstruation and postmenopausal osteoporosis, and the so-called interspinous ligament syndrome.

taken place. A period of more than 7 weeks should arouse suspicion of superimposed disease, such as arthritis or ruptured intervertebral disk, or of malingering.

Results of the roentgenologic examination are negative.

Muscle Rupture. When a muscle ruptures, a distinct gap can be felt between the retracted ends of the torn muscle and there is immediate disability consisting of local pain, loss of power, and swelling. Such a condition does not often occur in the spinal muscles.

Shoveler's Disease. Wetzel directs attention to the occurrence of avulsions of the spinal processes in the course of exertions, such as pitching hay in farm work, by persons who are unaccustomed to hard physical labor. The complaint is pain between the shoulder blades. There is sensitivity to pressure in this region, and forward and sideward lifting of the arms causes pains. The diagnosis is established by roentgenologic examination. Such patients should refrain for about 4 weeks from the exertion that caused the avulsion.

Degenerative Changes of the Vertebrae. The lumbosacral region is affected by degenerative changes to a greater extent, and at an earlier age, than the other regions of the spinal column, the cervical region being the next most susceptible.

Degenerative changes cause most of the backache in the lower portion of the lumbar segment, where stress is greatest. Degenerative changes are designated as wear-and-tear changes, osteoarthropathy, bony spurring and narrowing of the intervertebral disk

Degenerative changes in the spinal column are not limited solely to the bones. Degenerative changes occur in the skin, the subcutaneous fat, fascia, muscles, ligaments, tendons, bone and cartilage. The muscles soon lose their elasticity and ability for rapid co-ordination. The ligaments surrounding and supporting the spinal column degenerate more rapidly than the muscles. Changes in the vertebrae follow changes in the soft tissue

LUMBAR OSTEOARTHRITIS. In arthritis of the joints of the lumbar portion of the spinal column, pain may appear suddenly, as in lumbago, while the patient is stooping or in some disadvantageous position. Certain positions in sitting are avoided unless the lumbar portion is supported. The pain is intermittent and is characterized by acute exacerbations

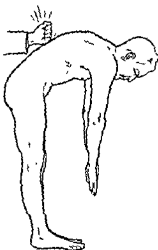


Fig 6-6. Percussion of the back

Examination usually reveals that the patient has evidence of lumbar joint disease and a superimposed myositis. The myositis accounts for the acute exacerbation Local tenderness may exist on either side close to the spinous processes or in the interspinous ligaments Percussion may localize the soreness definitely (Fig 6-6) The roentgenogram may not corroborate the clinical findings, since arthritis can seldom be visualized by the time the first symptoms appear.

Backache and Pain in the Back With Sciatica. Backaches may or may not be accompanied with extension of pain to the sciatic nerve and its distribution.

The term sciatica describes a chronic and often remittent pain situated low in the back which extends down the course of the sciatic trunk in the back of the thigh The pain may extend to the distribution of the external peroneal nerve to the lateral surface of the calf and finally to the foot

Some of the causes of the symptom, backache thus: (1) trauma; (2) rheumatoid arthritis and the cervical, or of the lumbar vertebrae, and dise: (4) malignant disease of the pelvic bones or vertebrae, or chronic osteomyelitis of

Nevertheless, the findings are constant and characteristic enough so that a presumptive diagnosis can often be made before intraspinal roentgenographic studies are made.

The diagnosis is made from properly interpreted spinograms. Love and Walsh warn of the danger of missing a protrusion of the disk on roentgenologic examination after injection of radiopaque oil unless the lumbar portion of the spinal column is kept in extension.

Malignant Metastasis to the Spinal Column. Pain is the first symptom It is almost always limited to definite segments supplied by the nerve roots passing outward through the foramina formed by the involved vertebrae The pain is aggravated by coughing, sneezing, yawning, straining at stool, bending movements of the spinal column or sudden jarring of the body.

The sufferer with metastatic lesions is reluctant to move or turn in bed because motion aggravates the pain Patients who have metastatic lesions of the spinal column are likely to walk the floor to avoid lying down Lying down often aggravates the pain

A common manifestation of metastasis of malignant disease to the spinal column is sciatica. Any sciatic pain occurring in a middle-aged patient; either unilaterally or bilaterally, which is not relieved by aspirin, arouses the suspicion of spinal metastasis.

A significant finding in those who have metastasis to bones is an elevated alkaline phosphatase content of the blood serum. In metastatic lesions of bone which result in increased, localized calcification (increased osteoblastic activity) the serum phosphatase levels are almost always elevated With destructive (osteoclastic) lesions, while the serum phosphatase values may be normal, they are frequently elevated

The diagnosis is suspected from the history and the examination Roentgenologic studies are of diagnostic value when two types of lesions are encountered. (1) evidence of increased osteoblastic activity, as indicated by localized areas of increased density due to increased calcification, (2) localized rarefaction, indicating increased osteolytic and osteoclastic activity with decalcification Increased concentrations of serum phosphatase are of diagnostic value.

History of Backache. It is essential to know (1) whether the pain in the back followed injury or unusual physical exertion, (2) the exact location of the pain, (3) whether the pain is continuous or recurrent, (4) what makes the pain worse, (5) what relieves the pain, (6) whether the pain is getting worse and (7) whether a lawsuit is pending or anticipated It is unfortunate, but nonetheless true, that this last question has to be included If there is litigation pending (and frequently the patient is reluctant to admit it) it is essential that full details, to include names, places and time, be obtained and be made a part of the written record.

Patients who complain of disabilities associated with the back have pain of one of two types, either static pain in the back or pain which recurs and lasts for periods of days or weeks with or without sciatic extension.

Static pain, the commonest of backaches, is brought on by use or physical activity, and it is relieved by rest Its presence denotes some fault in the moving parts of the back, either posttraumatic or due to degenerative disease of the joints There may be a congenital anomaly, or the back pain occurs in the absence of any demonstrable pathologic condition In these latter cases the pain is commonly due to poor postural attitudes which mechanically put undue stress on the ligaments, muscles and small joints of the back Static type of pain is usually present daily and does not vary in intensity except as the intensity of the physical activity varies As a rule, there are no severe acute episodes and there are no complete remissions. Static pain in the back may at times be accompanied by some degree of fibrositis, and the patient describes stiffness on arising, jelling with inactivity, or exacerbation

Of these backaches it is well to know that the backache which accompanies menstruation is rarely due to disease. If it is due to disease at all, the disease is intrinsic to the structures of the back or pelvis and proper examinations may detect the situation of the defective structures responsible for the pain.

Injury Involving the Spinal Column. When an injury of the spinal column has occurred, it is important, first of all, to determine whether or not the spinal cord or the spinal nerve roots have been injured This necessitates a study of the motility, the sensibility, and the reflexes (deep, superficial, pupillary and sphincteral). Should a neural disturbance be found, its exact site must be determined. The site of the vertebral injury causing the symptoms can then be deduced from the interpretations by a roentgenologist.

Protruded Intervertebral Disks. In recent years it has been demonstrated that protruded intervertebral disks are common causes of intermittent backache. The disks are ruptured by a sudden twist of the spinal column from a fall, or by other injury of the spinal column Rupture of a disk may occur also as a part of degenerative disease of the vertebrae A disk may be ruptured or protrude in any region of the spinal column from the first cervical vertebra to the last lumbar vertebra. However, rupture most commonly occurs in the lumbar region

The symptoms are characterized by episodic backache which usually comes on during back motion The pain is often incapacitating for a week or 10 days and then subsides. A recurrence of the pain is to be expected at some future date

During the attack coughing, sneezing and blowing the nose or straining accentuates the pain in all instances During the interval between the attacks there is no distress During an acute episode the patient cannot stand erect or sit comfortably and the pain may be worse at night than during the day These patients may or may not have pain in the leg However, pain is usually present in the leg and it may vary from a simple overflow of localized low back pain into the buttock to severe root pain that extends all the way down the leg into the toes There may be accompanying alterations in sensation, and paresthesias at times Rarely, there is some weakness or paralysis of peripheral muscles, and more rarely some interference with function of intestines or bladder

In the standing position there is often a true sciatic and disk scoliosis which presents as a bend principally affecting the lumbar vertebrae, and the shoulders are maintained at the same level by means of elevation of the pelvis on the affected side, [illegible]

an exacerbation of symptoms

Manipulation of the back in the sitting position may elicit little or no pain on rotation or lateral motion while the spinal column is flexed, but when it is hyperextended and these motions are repeated, all are painful Love and Walsh explain this symptom by their observation that the herniated disk is likely to be reduced by flexion of the lumbar portion of the spinal column, whereas hyperextension, on the contrary, causes the disk to protrude more markedly

The Achilles reflex, which subserves the fourth and fifth lumbar and first and second sacral segments of the spinal cord, is lost or diminished in more than one half of cases of disks at the lumbosacral junction Protruded disks at the fourth interspace are found to reduce the Achilles reflex in some cases, but protrusion at the third lumbar interspace decreases the ankle jerk in one half of these cases. The [illegible] of the [illegible] disk

is present at the third lumbar [illegible]

There are no physical, neurologic or orthopedic signs which are found in all cases of protrusion of intervertebral disks that are characteristic of this injury only.

MENSURATION. Measurement of chest expansion is indicated when ankylosing spondylitis is suspected. Measurement of the length of the legs may reveal a shortening which is influencing the spinal mechanics. The calves should be measured at their greatest circumference and the thighs at comparable measured levels below the anterior superior iliac spines.

The Sitting Position. Have the patient sit on a stool without a back, so that the feet rest comfortably and squarely on the floor. Observe the lumbar region for evidence of whether or not the weight is borne equally on the two ischial tuberosities. A manifest desire to sit on one ischial tuberosity and complaint of pain when asked to sit squarely on the stool arouse the suspicion that there is lumbosacral, sacro-iliac or coccygeal soreness.

If the normal lordosis of standing persists while sitting, the curvature may be at a higher level than usual because mobility of the lumbosacral joints is deficient, or it may be at the lumbosacral junction, as in spondylolisthesis

The Supine Position. An examining table long enough for the patient to lie at full length or one adjustable to full length is better than a shorter, higher table. If a stool is used to climb to the table, a patient with a unilateral back lesion will step up on the good leg

Ellis makes the following observations on patients as they get on the examining table. A diffuse tenderness in the lumbar region will cause the patient to crawl onto the table in the prone position and then roll over with some difficulty A patient who has coccygodynia objects to lying flat on the table. A patient who first sits on the examining table and then turns around so that a leg may be supported with his hands in bringing it up on the table is protecting a unilateral lesion on the side of the supported leg A lumbosacral or sacro-iliac soreness may prevent lying flat on the back on the table Lying is more comfortable if the leg and back are rotated slightly toward the painless side. The insistence on slight flexion of the hip while lying is more suggestive of sacro-iliac than of lumbo-sacral soreness Observe whether or not lordosis is changed by the patient flexing the hips and knees In lumbosacral soreness the lumbar lordosis does not change; in sacro-iliac soreness the lordosis is effaced

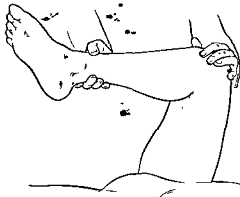


Fig 6-7 Internal rotation of hip joint is free of pain in the absence of disease of the hip

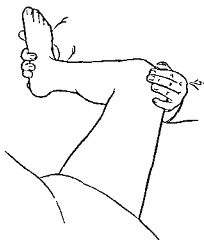


Fig 6-8 Lateral rotation of hip is free of pain in the absence of disease of the hip

Application of pressure on the knee during this manipulation with production of pain is a positive Laguere's sign (see text)

during cold, damp weather. The fibrositis in these instances is secondary to the underlying condition responsible for the pain, and is not the syndrome of primary fibrositis.

The recurring or intermittent type of pain in the back comes on in acute attacks. The attacks occur suddenly while the back is in motion. The pain may be incapacitating, may last from 5 to 10 days or more, and may recur 2 or 3 times annually. Such symptoms are commonly produced by protrusions of intervertebral disks, tumors of the spinal cord, spondylitis due to either tuberculosis or brucellosis, benign lesions or metastatic neoplastic conditions of the vertebrae.

Examination of the Back. The patient is examined in the standing, the sitting, the supine and prone positions Inspection of the normal back has been described (p. 186).

The Standing Position. The examination of the back begins by desiring the patient to walk, if walking is possible without too much pain. The examiner observes the manner of station and gait. The patient is then asked to sit down, take off the shoes and stockings. performance of these tasks also is observed. The patient who has a painful back moves carefully and with evidence of stiffness.

Usually the tilt of the trunk is away from the painful side in sciatic scoliosis, but occasionally it may be toward that side Observe whether or not there are flattening or the lack of lumbar lordosis, ankylosing spondylitis, prominent spinous process of the fifth lumbar vertebra in spondylolisthesis, angular kyphosis of Pott's disease, rounded dorsal kyphosis of Scheuermann's disease, and atrophy of the calf

MOTIONS OF THE SPINAL COLUMN The motions of the spinal column are extension, flexion, rotation and lateral bending The ranges of these motions are determined while the knees of the patient are held straight

A limitation in flexion of the spinal column in the standing position should be compared with the range of motion at which the pain appears when these same motions are performed when the patient is sitting normally upright.

Lateral motion in the lumbar region is confined to an arc of not more than 40 degrees. The extent of active and passive lateral motions is compared with this normal range. The lateral motions of the lumbar vertebrae are better observed with the patient in the sitting position than in the standing position In the standing position spasm of the tendons bounding the popliteal space may cause a limitation of motion

Flexion and extension are free movements of the neck and lumbar regions. Rotation is free at the articulation of the axis with the atlas. It is limited in the midcervical region, freer in the upper portion of the thoracic region, gradually diminishes downward, and is absent in the lumbar region.

The degree of referred pain, if any, on each motion is significant as an aid to the localization of disease On flexion the patient will stoop toward the side of the spastic erector spinae group of muscles, which is ordinarily toward the side of the pain

Record should be made as to which of these motions, if any, reproduces the pain of which the patient complains. In the matter of forward flexion one should distinguish between movement in the spinal column itself and movement accomplished by flexion at the hip joints

PALPATION. Palpation and percussion over the spinous processes, lumbosacral and sacro-iliac joints should be carried out. The amount of spasm of the paravertebral muscles is estimated. One should ascertain whether or not there is tenderness on pressure over the sciatic notches or over the sciatic nerve itself in the thigh. In fibrositis the demonstration of palpable tender nodules is diagnostic.

PERCUSSION. Percussion of the back is usually performed with the closed fist (Fig 6-6).

LASÈGUE'S SIGN. The (modified) straight leg-raising sign of Lasègue is elicited by elevating the limb with the knee extended. Approximately the first 20 degrees of this motion produces flexion of the hip and may produce pain in the hip joint. As the motion continues and a pull is exerted on the ischial tuberosity by the hamstring muscles, rotation is exerted on the sacro-iliac joint When the leg approaches a vertical position or points straight upward, torsion increases rapidly and begins to be strongly transmitted through the lumbosacral joint of the same side. At right angle flexion even soreness in the opposite lumbosacral joint will begin to be manifest.

In sciatica, if the straight leg test is performed to the point where pain begins, sudden dorsal flexion of the ankle will greatly aggravate the symptoms (Fig. 6-12).

LAGUERRE'S SIGN This sign is elicited by flexion, abduction and outward rotation of the hip These movements force the femoral head against the anterior portion of the capsule, and pain results if there is hip-joint disease. This test is used to distinguish psoas spasm, hip-joint disease and sacro-iliac disease from lumbosacral disease (Fig. 6-8)

GAENSLEN'S SIGN Gaenslen's test is used to elicit soreness in the sacro-iliac joint.

the table with the knee flexed Pain is produced by rotation of the sacro-iliac joint of the hyperextended leg

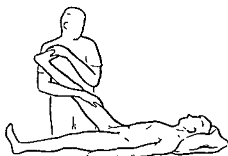


Fig 6-12 Lasègue's test Straight leg-raising test with knee kept extended while pressure is applied to the foot

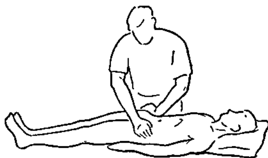


Fig 6-13 Sacro-iliac tenderness demonstrated by downward pressure on the iliac crests.

able range, so that, when pain begins in the lumbosacral region, as soon as flexion begins, sooner than when either leg is raised separately, the suspicion of disease rests on the lower lumbar portion of the spinal column and lumbosacral joints rather than on the sacro-iliac joint and the sciatic nerve

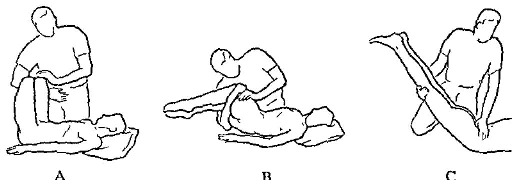
the flexed knee down

BAER'S SACRO-ILIAC POINT OF TENDERNESS Before concluding the examination in the position for eliciting Patrick's sign, palpation should be made deeply in each lower quadrant of the abdomen to elicit Baer's sacro-iliac point of tenderness, which is described as situated 2 inches from the umbilicus on a line between the umbilicus and the anterior superior iliac spine Sacro-iliac tenderness may also be elicited by downward pressure on sacro-iliac spines (Fig 6-13)

The Prone Position. When it is possible for the patient to lie in this position, the examination should be continued as an inspection to estimate (1) the amount of lateral deviation as compared with that present in the standing and sitting positions, if any exists, and (2) the degree to which such distortion of the spinal column

HIP MOTION. When the knee is flexed, motions of the hip joint can be studied without the transmission of tension to the sacro-iliac or the lumbosacral joints. Any complaint on internal or external rotation at the hip *with the hip and knee flexed* directs suspicion to the hip joint itself. The motions of the hip joint may be tested as shown in Figures 6-7 and 6-8

Lateral and rotary motions of the lumbar portion of the spinal column, while the hips and the knees are flexed, are performed by the examiner pressing the knees forward, laterally and downward as desired (Fig. 6-9). Passive flexion of the lumbar



Modified from Ellis, J. D., *The Injured Back and Its Treatment*, Charles C Thomas 1940

Fig 6-9 A, flexion and rotation of the hips may identify lumbosacral soreness as well as the extent of spasm or contraction in sciatic scoliosis In acute injury of a sacro-iliac joint compressive force (forceful flexion of both hips) is not so painful as axis traction or separation

B, in lumbosacral joint disease strain on the sacro-iliac joints, exerted as shown, elicits tenderness in the lumbosacral joint.

C, fixing the spinal column and hyperextending the legs permit observation of the position at which pain begins The force acts successively on the lumbosacral junction, the sacro-iliac joints and up the spinal column as the point of fixation is moved upward

joints can be performed through a larger arc with less pain in the supine position than in the standing or the sitting position. Compression of the anterior superior spines of the ilia toward each other and separation from each other as tests for sacro-iliac disease are performed in this position. In sacro-iliac disease these two maneuvers cause a complaint of pain

The straight leg-raising tests are most valuable in detecting disease of the sacro-iliac joint and disease of the lower lumbar region of the spinal column (Figs. 6-10 and 6-11).

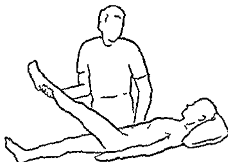


Fig 6-10 Straight leg-raising test Hip free. This much flexion at the hip is usually without pain when *the hip is not diseased*



Fig 6-11. Straight leg-raising test with hip held down Less flexion at the hip is permissible without the production of pain when the hip is *held down than when it is free*

nates in the subclavian vein, which lies to the inner (anterior) side of the artery.

Immediately below the clavicle is a depression, the infraclavicular fossa. On the sternal side of this depression can be felt the first rib. Since ribs are not always easily identified, it is best, in counting them, to locate the angle of the sternum (angle of Ludwig). The second rib is immediately opposite this angle The angle of the sternum is about 2 inches (5 cm) below its upper edge. Attached to the lower edge of the inner half of the clavicle is the pectoralis major muscle, and to the outer third, the deltoid muscle

Only a small part of the lower edge of the clavicle is free from muscular attachments This muscle-free edge forms the base of the *subclavicular triangle*, and its two sides are formed by the adjacent edges of the pectoralis major and deltoid muscles. This triangle marks the course of the underlying first portion of the axillary artery with the vein and the cords of the brachial plexus of nerves. Deep pressure appropriately applied here can compress the axillary artery against the second rib, but not so effectively as above the middle third of the clavicle. The pressure on the artery is immediately manifested by tingling along the inner side of the arm

Just to the outer side of the junction of the middle and outer thirds of the clavicle, in front of the deepest part of the concavity, is the coracoid process of the scapula It is best felt by pressing the fingers flat on the surface. Running from the coracoid to the acromion process is the sharp edge of the coraco-acromial ligament.

Beneath the acromion process, but covered by the deltoid, is felt the greater tuberosity of the humerus If the arm is placed alongside the body with the palm facing forward, a distinct groove can be felt to the inner side of the acromion process. It is the bicipital groove of the humerus for the long tendon of the biceps muscle. The greater tuberosity of the humerus projects beyond the acromion process and forms the prominence of the shoulder On rotating the arm, the greater and lesser tuberosities of the humerus can be distinctly felt moving under the deltoid muscle

The acromion process of the scapula posteriorly forms a distinct angular prominence where it joins the spine of the scapula This prominent angle can be seen and felt and is used as a landmark for measuring the length of the humerus The spine of the scapula ends at the posterior border of the scapula This border is opposite the fourth rib and the third thoracic vertebra With the arm to the side, the lower angle of the scapula lies over the seventh interspace

THE SHOULDER

Muscles. The shoulder embraces two sets of muscles one set connects the shoulder girdle with the trunk, and the other, the humerus with the shoulder girdle

Movements. The main movements of the shoulder girdle are anteroposterior, as in swinging the arm, those of abduction and adduction, as in raising and lowering it sidewise, and rotary

Functional Testing of the Muscles of the Shoulder. *Deltoid* The examiner, standing in front of the patient, requests the patient to raise the arms laterally to a horizontal position Inability to do so indicates deltoid paralysis Also the deltoid muscle may be conveniently tested as shown in Figure 6-14. (Circumflex nerve supply, C_5, C_6)

Pectoral The examiner stands in front while the patient stretches out the arms straight in front: the examiner then approximates the patient's hands against resistance of the pectoral muscle Paralysis is indicated by failure of contraction.

The two parts of the muscle are tested the sternocostal part as depicted in Figure 6-15, and the clavicular part, as in Figure 6-16. (Lateral and medial pectoral nerve supply, C_5, C_6)

Latissimus Dorsi The patient raises the arms laterally to a level, then, while keeping them fully extended, brings them downward and backward, as if to make

can be corrected after attempting to pull down the leg on the concave side of the lumbar curve.

Roentgenograms. No examination of the back is complete without anteroposterior and lateral roentgenograms of good quality. A localized lateral roentgenogram of the lumbosacral joint is necessary when a lesion at this site is suspected. In fact, when the nature of a lesion is doubtful, localized anteroposterior and lateral roentgenograms of any part of the spinal column are indicated. Oblique views are useful when one suspects a lesion of the articular facets or open neural arches in cases of spondylolysis and spondylolisthesis. When a lesion of the sacro-iliac joint is suspected, stereoscopic anteroposterior roentgenograms of the pelvis will give the most information.

Patients with ruptured intervertebral disks may require myelographic examination.

SUMMARY OF BACKACHE

Many backaches are left unexplained after all examinations have failed to reveal disease. Most persons who have these unexplained backaches continue to live normal active lives despite the back pain.

Perhaps the two commonest ailments to cause soreness and pain in the back are fibrositis and psychoneurosis In women backache is rarely due to disease of the pelvic organs

In a patient known to have malignant disease, an unexplained backache, especially if there is sciatic distribution of the pain, or extension of pain to the leg, excites the suspicion that the cause of the pain is metastasis to the spinal column

In a middle-aged person the onset of a backache with sciatic distribution which is not relieved by aspirin excites the suspicion that there is metastasis to the spinal column from an unknown malignant source The suspicion is strengthened if there is bilateral distribution of the pain

THE APPENDICULAR SKELETON AND LOCOMOTION

THE SHOULDER GIRDLE (CINGULUM EXTREMITATIS SUPERIORIS) AND THE UPPER EXTREMITY

Topography and Bones. The shoulder girdle projects the arm well out from the trunk by means of a framework which consists of three bones the clavicle and scapula superiorly, and the humerus inferiorly. These bones form the basis of the shape and topography of the shoulder. The shape may be modified by the muscles and fat

The clavicle is subcutaneous and can be felt throughout its length. The medial end normally projects above the upper edge of the sternum, which can be felt at the suprasternal notch A prominent ridge marks the outer extremity of the clavicle, if this ridge is difficult to recognize, as is often the case, the examiner continues directly laterally to the point of the shoulder, which is formed by the tip of the acromion process This point having been recognized, the end of the clavicle is found directly mediad from it.

In the median line above the sternum is the suprasternal notch. Just to each lateral edge of the notch is the prominent sternoclavicular joint. On the right side this joint marks the ending of the innominate artery and the commencement of the right common carotid and subclavian arteries That on the left marks the left carotid with the subclavian directly to its outer side and a little posteriorly.

The medial two thirds of the clavicle is convex anteriorly. The lateral third of the clavicle is convex posteriorly, and from its superior surface the trapezius muscle can be felt. Just above the clavicle in the neck and behind the clavicular origin of the sternocleidomastoid muscle is seen the external jugular vein. It termi-

scapulae as close together as possible (Fig 6-21). (Accessory nerve supply, C_3, C_4.)

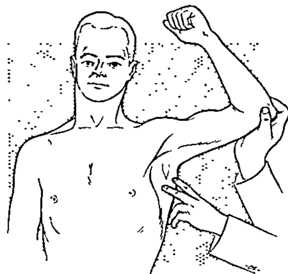


Fig 6-17 Latissimus dorsi muscle (insertion) Standing or sitting with the arm horizontally and laterally extended Attempts are made to extend the arm against resistance The muscle can be seen and palpated with the middle finger Nerve supply C_6, C_7, C_8

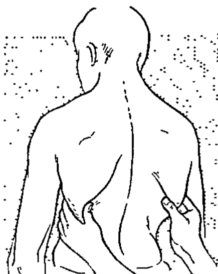


Fig 6-18. Latissimus dorsi muscle (posterior portion) Standing or sitting. On coughing the muscle can be felt except in extremely obese persons. Nerve supply C_6, C_7, C_8

Rhomboideus Muscles. The patient moves the shoulder backward against resistance (Fig 6-22) (Nerve supply, C_4, C_5)

Supraspinatus Muscle Standing with the arm by the side, attempts are made to abduct the arm against resistance. The muscle can be felt on top of the shoulder (Fig 6-23A) (Suprascapular nerve supply, C_5)

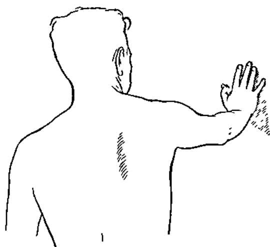


Fig 6-19 Serratus anterior muscle While standing with hand against wall, patient pushes forward. The medial border of the scapula remains close to the thoracic wall, which can be seen or felt Nerve supply C_5, C_6, C_7

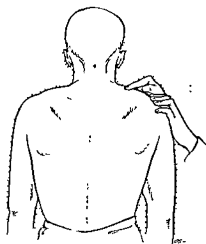


Fig 6-20. Trapezius muscle (upper part) Standing or sitting Attempts are made to elevate the shoulder against resistance The midportion of the muscle can be seen and felt Nerve supply C_3, C_4 (accessory nerve, eleventh cranial)

the hands meet behind the sacrum. The examiner stands behind the patient to resist the movement The muscles are also conveniently tested as the patient tries to adduct the horizontally and laterally extended arms against resistance (Fig 6-17). If the

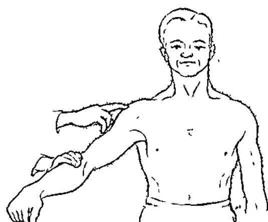


Fig 6-14. Deltoid muscle. Standing or sitting *Attempts are made to maintain an* angle of abduction of the arm of more than 15 degrees against resistance The muscle can be seen and felt Nerve supply C_5, C_6 (circumflex nerve)

patient coughs, the muscle bellies can sometimes be seen and palpated (Fig 6-18). (Nerve supply, C_6, C_7, C_8)

Serratus Anterior Request the patient to push with his hands against the wall If the serratus has lost its power, the scapula will project, and the digitations of the muscle, which should be visible, will not be seen (Fig. 6-19). (Nerve supply, C_5, C_6, C_7.)

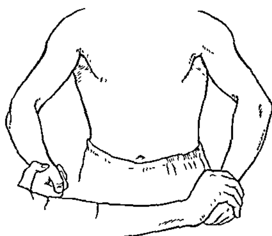


Fig 6-15. Pectoral muscles (sternocostal portion) The patient standing or sitting. The arms are raised below the horizontal Attempts [illegible] the arms against resistance [illegible]

pectoral nerves)



Fig 6-16 Pectoral muscles (clavicular portion) Standing or sitting *The* arm is raised above *the horizontal* and forward flexed at the elbow *Attempts* are made against *resistance to* abduct the arm The clavicular and usually the costal parts of the muscle are evident. Nerve supply C_5, C_6, C_7, C_8 (lateral and medial pectoral nerves).

Trapezius. The examiner asks the patient to raise the shoulder upward against the pressure of the examiner's hand. This will demonstrate the strength of the upper part of the trapezius (Fig 6-20). The examiner asks the patient to bring the

other causes for shoulder pain. Some of these causes are intrinsic while others are extrinsic and these may be enumerated as (1) arthritis (rheumatoid and osteoarthritic, tuberculous and due to pyogenic infections), (2) tumors and infections of the scapula or head of the humerus, (3) lesions of the clavicle, (4) lesions of the acromioclavicular joint, (5) tumors of the soft tissues about the shoulder, (6) fractures or fracture dislocations of the shoulder and (7) diseases of the diaphragm, which often cause pain in the shoulder.

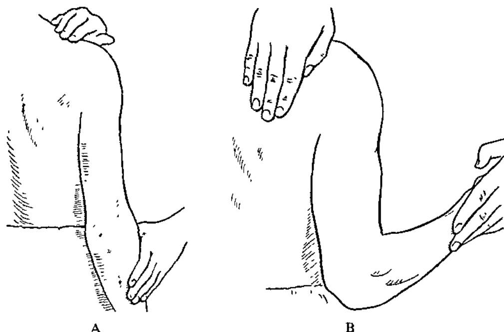


Fig 6-23 A, supraspinatus muscle Standing with arm by the side, attempts are made to abduct the arm against resistance The muscle can be felt on top of the shoulder Nerve supply C_5 (suprascapular nerve)
B, infraspinatus muscle Standing or sitting with the elbow flexed to the side, resistance is made against attempts to rotate the arm externally at the shoulder joint The muscle can be felt Nerve supply C_5, C_6 (suprascapular nerve)

The differential diagnosis of lesions of the shoulder from lesions of the cervical portion of the spinal column or brachial plexus often is difficult It is recalled that in cases of pain in the shoulder or arm, lesions of the cervical part of the spinal column and shoulder joint may be present The most important point in differential diagnosis is the presence of local signs in the shoulder, that is, both active and passive limitation of motion, either diffuse or localized tenderness; atrophy of variable severity, and swelling or local heat in an occasional case of acute bursitis. In cases in which the shoulder joint is free of all of these signs, the primary cause of the trouble usually is elsewhere The pain is referred pain

A number of lesions of the thorax and a few of the abdomen which irritate the [illegible]

erred

pain

Lesions of the superior pulmonary sulcus adjacent to the brachial plexus or sympathetic chain also may cause pain of the arm. Pancoast described a syndrome including roentgenographic shadow [illegible] tumor at the apex of the lung, a neuritic type of pain of the arm, atrophy of [illegible]scles of the hand and arm and Horner's syndrome The *Pancoast syndrom*[illegible] a distinct clinical entity, since neuro-

Infraspinatus Muscle. Standing or sitting with the elbow flexed to the side, resistance is made against attempts to rotate the arm externally at the shoulder joint. The muscle can be felt (Fig. 6-23B). (Suprascapular nerve supply, C_5, C_6)

MONARTICULAR DISORDERS

These affect, intra- or extra-articularly, a single shoulder, elbow, hip or knee.

The Shoulder and Monarticular Disorders. The etiologies of the monarticular involvements, the syndrome or syndromes of arm pain and their relation to lesions of the cervical part of the spinal column, shoulder and brachial plexus are not always possible to delineate and to elucidate.

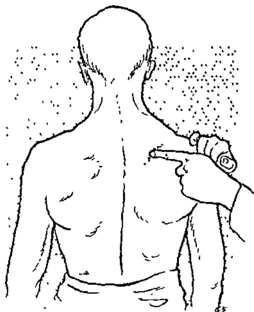


Fig 6-21 Trapezius muscle (adductor scapulae portion) Standing or sitting Attempts are made to carry the shoulder backward against resistance The lower part of the muscle can be felt and often seen Nerve supply C_3, C_4

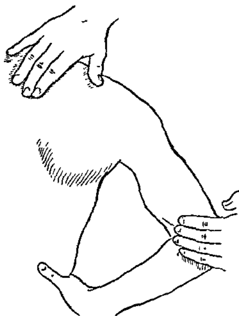


Fig 6-22 Rhomboideus muscles Patient standing, elbow flexed and extending laterally with hand on hip tries against resistance to brace shoulder backward The muscle can be seen and felt Nerve supply C_4, C_5

The painful lesions of the shoulder due to a slowly developing internal derangement, some of which are associated with trauma, others not, are (1) frozen shoulder, capsulitis, tendinitis, peritendinitis or periarthritis, (2) calcified subdeltoid bursitis or degeneration of the supraspinatus tendon and (3) tears of the supraspinatus tendon and of the musculotendinous cuff. Regarding these painful shoulders certain facts as enumerated by Ghormley have come to be accepted. 1. The supraspinatus tendon tends to degenerate and the frequency of this occurrence increases with age. 2. There is general agreement that the so-called *periarthritis* or *frozen* shoulder has its inception in inflammation of the tendon or tendon sheath 3 Calcification in bursae probably results from accumulation of degenerated tendinous material. 4. Ruptures of the supraspinatus tendon are fairly common in older persons. They may cause severe symptoms in some cases and require surgical treatment. 5. Among younger persons, subsequent to trauma, tears of the musculotendinous cuff are much more severe and serious than among older persons

In addition to these facts enumerated by Ghormley, Bickel has enumerated

with hypesthesia, paresthesia or anesthesia In time atrophy of the muscles of the hands supervenes. If the pressure and circulatory insufficiency are allowed to continue, pressure on the subclavian artery decreases the volume of the radial pulse. Peripheral thrombosis may occur and may be so extensive that gangrene ensues.

EXAMINATION. Palpation of the supraclavicular fossa is made in an attempt to detect a *cervical rib or any difference in the prominence of the structures in the* fossa and tenderness on pressure over the scalenus anticus muscle Pressure over this muscle causes extension of the pain down the ulnar side of the arm.

The two radial pulses are examined for evidence of differences in the volumes While palpating the radial pulse, request the patient to turn the head upward toward the affected side, to inspire and to hold the breath. If there is abnormal pressure by the scalenus anticus muscle on the artery, the pulse volume will be decreased or the pulse may be obliterated and the symptoms will be reproduced.

DIAGNOSIS. The diagnosis of the scalenus anticus syndrome is based on the presence of pain, atrophy, circulatory abnormalities and disturbance of sensation in the *upper extremity. The presence of cervical ribs is not sufficient evidence to warrant* a diagnosis of the scalenus anticus syndrome since, as stated, cervical ribs usually do not present symptoms

DIFFERENTIAL DIAGNOSIS The differential diagnosis of scalenus anticus syndrome requires a consideration of the following: (1) brachial neuritis; (2) Raynaud's disease, (3) thromboangiitis obliterans (Buerger's disease); (4) subacromial bursitis; (5) protrusion of a cervical intervertebral disk, and neoplasms of the cervical portion of the spinal cord, and (6) cervical spondylitis

THE AXILLA

Have the patient raise the arm directly out from the body. The armpit and axillary folds are thus made visible

The axilla is a wedge-shaped space with its apex upward, formed between the arm and chest at their junction It serves as a passage for the arteries, veins, nerves and lymphatics between the trunk and the upper extremity It is frequently the site of growths and abscesses

The rounded edge of the anterior axillary fold is formed by the pectoralis major muscle. It follows the fifth rib, and its upper end merges with the lower edge of the deltoid muscle The posterior fold is formed by the latissimus dorsi and teres major muscles By deep upward pressure with the extended approximated fingers in the axilla, the rounded head of the humerus can be felt.

Lymphatic structures of the axilla, especially the axillary lymph nodes, combined with a few scattered nodes in the antebrachium and the brachial regions, drain the entire upper extremity The axillary nodes receive the afferent vessels from the anterior and the lateral aspects of the thoracic wall, from the breast, and posteriorly from the scapular region These axillary nodes are anatomically situated in two groups, the axillary nodes proper and the subclavian nodes

The lymphatics of the middle and lower portions of the back as low down as the umbilicus also drain into the axilla

These lymph nodes communicate with one another The part affected ordinarily drains to the nearest nodes Occasionally, however, the infection may pass by or through one set of nodes without causing enlargements and may involve a neighboring communi- [illegible] or scapular [illegible]

[illegible] are always palpable When they are not enlarged, they cannot all be found. The size of the normal lymph nodes is usually inversely proportional to the number of nodes present In an axilla in which there are few nodes some of these may be palpable normally

The subclavian nodes lie in the infraclavicular triangle between the pectoralis major

fibromas or inflammatory lesions as well as malignant lesions may cause it. Pain from lesions of the esophagus is rarely referred to the arm. Diaphragmatic lesions, however, may cause pain in the arm. This is particularly true of lesions of the central portion of the diaphragm, such as esophageal hiatal hernias. Diaphragmatic pleurisy or irritation also may cause pain in the shoulder and arm.

Ankylosis of the Shoulder. The relative loss of co-ordination, endurance and security in respect to the duties of the arm and hand will vary according to the extent the ankylosis approaches or departs from the more favorable position of about 50 to 60 degrees abduction (McBride).

Partial Ankylosis. Partial limitation of motion in the shoulder is often due to a periarticular derangement of tissues resulting from trauma such as contusion and fractures of the head or surgical neck of the humerus A sprain or dislocation may leave permanent damage to the capsule and ligaments of the joint. Habitual dislocation is not commonly associated with a painful or stiffened joint The supraspinatus muscle or tendon may be ruptured, and if so the rupture is difficult to recognize

Continuous immobilization with the arm to the side will result in permanent contraction of the adductors and atrophy of the deltoid, so that there is no power to lift the arm outward Paralysis of the deltoid may follow a fall directly on the shoulder which injures the circumflex nerve Such a paralysis may be permanent

Suppuration and persistent sinuses may exist for many months after a compound fracture of the shoulder Movement of the joint will be greatly hampered Osteomyelitis may follow a compound fracture and may cause permanent disability Adhesions from this source do not respond well to manipulation

A rheumatic fibrositis may complicate injury to the shoulder. When it does, the pain is persistent and improvement is slow A deltoid bursitis may occur spontaneously or be induced by injury There may be a tenosynovitis of the long head of the biceps to add more to the pain and disability

When the scapulohumeral joint is ankylosed, shoulder joint action is completely lost if there is no movement of the scapula Ankylosis is incomplete if the scapula is free With fixation of the arm at the side there is complete loss of motion. The hand can perform its functions in the sagittal plane only by means of the forearm, and the center of action is now situated at the waist instead of in the shoulder.

When the scapula is free, there is considerable freedom of motion rendered through the gliding of the scapula and through the sternoclavicular joint. The amount of motion afforded through the scapula greatly lessens the severity of rigid ankylosis in the scapulohumeral joint.

When fixation of the shoulder joint occurs with the arm more than one half abducted and slightly flexed with rotation at midpronation, it is in a useful position. This position permits more flexibility at the shoulder while lifting than other positions permit. When the scapula is fixed, the disability is much more severe than when it is free.

The Scalenus Anticus Syndrome With and Without Cervical Rib. The scalenus anticus syndrome may be associated with a cervical rib or it may occur spontaneously The symptoms are attributable to irritation and compression of the [illegible]

produce symptoms. These ribs occur unilaterally or bilaterally and [illegible] length.

SYMPTOMS The commonest and often the first symptom is a sharp pain originating from a sudden rotation of the head or from a forceful downward pull of the shoulder. In the intervals between these sharp pains there may be a dull, aching, burning and boring pain occurring during the latter part of the day or with fatigue. The pain extends the length of the inner side of the arm and may be associated

Projecting on each side of the elbow are the two epicondyles of the humerus These bony projections do not belong to the forearm. The two epicondyles are nearly on the same level. The medial (internal) is the more prominent. By deep pressure the lateral (external) supracondylar ridge can be felt running up the arm somewhat posteriorly from the lateral (external) epicondyle. The medial (internal) supracondylar ridge is much less easily felt. When the elbow is flexed at a right angle, a plane parallel with the humerus passes through the two epicondyles and the tip of the olecranon. If the forearm is extended, the olecranon passes somewhat in front of this plane. Hence in examining the elbow for injury it is desirable to determine the relation of these points when the elbow is bent at a right angle.

The elbow is now examined while the arm is extended. In this position the tip of the olecranon can be felt with the medial (inner) epicondyle to its inner side. Between the medial and lateral epicondyles is a deep groove and in this groove can be felt the head of the radius.

On the posterior aspect of the elbow joint is the ulnar nerve. A bursa lies between the upper or posterior surface of the olecranon and the skin; and also another on its inferior surface, extending downward, which from its exposed position is frequently injured and enlarged Such an enlargement occurs from chronic irritation in certain occupations (as mining), hence the name miner's elbow

In the middle of the flexor surface of the elbow below the crease is a depression called the antecubital fossa. To its outer side is the muscular prominence of the extensors and supinator. To its inner side is the muscular prominence of the flexors and pronator The inner muscular swell ends at the medial (internal) condyle, but the external one passes well up on the arm.

The *antecubital fossa* or space is occupied by a number of *veins* which are of importance because they are frequently used for purposes of parenteral medication, sometimes for blood transfusions, and not infrequently they are wounded and give rise to hemorrhage.

The Elbow and Monarticular Disorders. The diseases of the region of the elbow include inflammatory processes and neoplasms Inflammations of the elbow and its neighborhood may be acute or chronic. In *acute arthritis* the whole circumference of the joint is tender on pressure, the swelling being most marked where the capsule is most superficial

Chronic arthritis of the elbow joint may be due to rheumatoid arthritis, tuberculosis or syphilis. An arthritic involvement is not likely to be confused with simple chronic bursitis olecrani or with epicondylar neuralgia.

Of the *tumors* of the region of the elbow, those of intramuscular origin include angioma and sarcoma. The simple muscle hernia due to the bulging of contracted muscle through a defect in the aponeurosis of a muscle, following trauma or congenital defect, is easily distinguished from neoplasm. Similarly, calcification within a muscle following trauma, the so-called traumatic osteoma, in reality a circumscribed ossifying myositis, is differentiated from tumor by the history of trauma and by roentgenographic examination, the appearance in roentgenograms is distinctly characteristic.

Tumors originating in the nerves rather than in the muscles can be differentiated from muscle tumors by their position in the course of the nerves and by their spindle shape They consist usually of neurofibromas, more rarely of sarcomas.

Inflammations of the bones may be acute (osteomyelitis) or chronic (chronic staphylococcal osteomyelitis, sporotrichosis, tuberculosis or gumma). The neoplasms of the bones found in the region of the elbow are most often myeloid sarcomas; occasionally other forms of sarcoma, fibroma or enchondroma may be met with.

Ankylosis of the Elbow. The function of the elbow is to serve the hand and

and deltoid muscles and on the front of the subclavian vein above the pectoralis minor muscle. They receive radicles from the mammary gland as well as from the axillary groups. They receive the overflow either directly or indirectly from all the other lymphatics of the foregoing regions They may empty through the subclavian trunk into the subclavian vein near its junction with the external jugular vein or into the right jugular vein. These nodes may be palpable in the presence of carcinoma of the breast.

Axillary Tumors. Tumors of the axilla are almost always due to involvement of the lymph nodes They may be inflammatory, forming the ordinary axillary adenitis, they may be tuberculous, or they may be malignant. Since the tumors of the axilla are often due to disease of the lymph nodes, the parts which the nodes drain should be searched to determine *the starting point of the disorder.*

Chronic infections of the glands of the skin cause tender axillary indurations. Lipomas, accessory breasts or breast tissues may be present in the axilla, but more commonly these occur along its anterior margins.

THE ARM

The arm has four sets of muscles to perform its four directional movements These sets of muscles are (1) the lateral group (abductors), (2) the internal group (adductors), (3) the anterior group (flexors) and (4) the posterior group (extensors)

The deltoid forms the large rounded prominence of the shoulder. At its insertion the humerus is nearest the surface and easily palpable The posterior edge of the deltoid can be plainly seen, when contracted, running upward and inward and crossing the posterior fold of the axilla at right angles. Its anterior edge blends more or less completely with the pectoralis major

The *biceps brachii and the brachialis form the muscular mass on the anterior* surface of the arm. The *posterior* or extensor set of muscles includes the triceps

On the medial aspect in the lower third of the arm the brachial artery is covered only by the skin and superficial and deep fascia, and can be felt pulsating along the inner edge of the biceps muscle and tendon, it can be compressed against the bone by pressure directed outward At this point tourniquets may be applied

THE ELBOW JOINT

The elbow joint is a hinge joint The articulation between the trochlea and the ulna is so shaped as to allow no lateral motion, but only an anteroposterior one. The forearm can be extended to an angle of 180 degrees, or in a straight line with the arm It can be flexed to an angle of 30 to 40 degrees Sometimes it cannot be flexed so much, so that if after an injury to the joint the patient can flex the elbow to half a right angle, this may be regarded as the normal amount of motion

The axis of motion of the elbow joint (the radial aspect anteriorly) slopes slightly from the lateral side downward and inward. The effect of this slope is to give a slight obliquity to the motions of flexion and extension This obliquity is not noticeable except in extreme extension and flexion When the forearm is completely extended (palm forward) it is seen not to lie in the axis of the arm but to bend outward from the elbow at an angle of 170 degrees. This angle is called the *carrying angle* because, by resting the elbow against the side, any article which is carried in the hand, as a bucket of water, is kept away from the lateral aspect of the leg.

In *examining the elbow* it first should be flexed at approximately a right angle. The prominent olecranon process is the posterior projection of the elbow. It is subcutaneous, and it can be felt and followed down the back of the forearm. From the tip upward for a comparatively short distance can be felt the upper surface of the olecranon, into which the triceps inserts To feel this upper surface distinctly, *the forearm should* be somewhat extended to relax the triceps so that the outline of the upper portion of the olecranon is distinctly palpated

ample, the screw driver). These instruments are therefore designed for right-handed individuals. A left-handed individual's greatest handicap is that of having to use instruments which were not designed for him.

THE WRIST

There is a bony prominence on each side of the wrist caused by the expanded lower end of the radius on the side of the thumb (medial) and head of the ulna on the side of the little finger (lateral) The medial (inner) prominence is exemplified by abducting the hand, the lateral (outer) prominence of adducting it.

Proximal to the wrist on the anterior and medial part can be felt the sharp and prominent distal 1 inch (about 2.5 cm) of the radius Following the bone distally on its medial side, one feels the tip of the styloid process, a most important landmark The styloid process is in the anatomist's snuffbox (tabatière anatomique), a depression on the dorsal aspect of the wrist, just below the radius

Between the tip of the styloid process of the radius and its sharp anterior border are the extensor ossis metacarpi pollicis and extensor brevis pollicis tendons. The sheaths of these tendons frequently become inflamed from injuries. If the examining hand is placed firmly on the lower portion of the radius of a patient so affected, and the patient moves the thumb, a characteristic grating irregularity of movement of the tendons can be palpated as they move in their inflamed sheaths.

If the posterior surface of the ulna is followed downward, the styloid process forming its extremity can be distinctly felt, especially if the patient's hand is placed in the supine position and slightly flexed

The styloid process of the radius extends lower than that of the ulna Across the central (palmar) surface of the wrist there are two transverse lines The proximal or upper one corresponds to the wrist joint The distal or lower one corresponds to the joint between the two rows of carpal bones.

On the dorsal surface of the wrist when in pronation, one third of the width of the wrist across from the edge of the radius, can be felt a bony prominence. This prominence marks the middle of the posterior surface of the radius The radius occupies two thirds of the dorsal surface of the wrist, and the ulna the other third; by firm pressure the interval between the bones can be felt

The wrist joint has no movement of rotation Rotation of the hand is accomplished by pronation or supination of the forearm The hand can be flexed and extended through an arc of approximately 140 degrees, and adducted and abducted about 70 degrees. Adduction or bending toward the ulnar side is much greater than abduction or movement toward the radial side

The extent of the movements of the wrist varies individually.

Ankylosis of the Wrist. The function of the wrist is to serve the fingers and hand in carrying out such duties as reaching, pointing, grasping, pinching, holding, pushing, pulling, striking, carrying, swinging, throwing, turning and lifting The hand and fingers, in execution and achievement of their appointed functions, require the elbow and shoulder to serve their purposes

The causes of partial or complete ankylosis of the wrist are contusion or sprain, tenosynovitis or ganglion, fracture and dislocation, suppuration, continuous and prolonged immobilization, scar contraction and shortening of muscles, paralysis and rheumatic fibrositis

Partial Ankylosis. Sprains are often accompanied by prolonged disability and may result in permanent loss of function Effusion into the wrist joint often hampers the joint motion for long periods of time if not permanently. Sprains may be distinguished from tenosynovitis by the limitation of the swelling at the joint lines and do not extend up and down in the direction of the tendons In traumatic synovitis there is an aseptic effusion of blood and serum into the joint, and in case of the wrist joint there are so many pouches and cartilaginous reflections about the carpal

arm in carrying out the motions entailed by reaching, pointing, holding, pushing, pulling, striking, carrying, swinging, throwing, turning and lifting.

Ankylosis of the elbow joint may result from dislocations, contusions, suppurations, prolonged immobilization, scar contracture, myositis ossificans and rheumatic fibrosis.

Partial Ankylosis. When the range of elbow motion is less than a right angle, the arm, which is subservient to the hand, does not provide flexibility. Any motion at all is preferable to rigid fixation; motion from 90 degrees to 35 degrees flexion is useful in the lighter activities but such motion will not permit carrying, pulling or pushing heavy objects.

When the range of motion of the elbow joint is from 180 to 80 degrees, the greater portion of the requirements for accommodation of the hand and arm are fulfilled In the performance of the motions required for lifting, pushing, pulling or carrying, the angle approaching 120 degrees is more desirable than a right angle (McBride)

When the elbow joint action is lost, the arm is stiffened solidly. The stiffened arm and the hand have their fulcrum at the shoulder, and can perform only as far as the shoulder muscles are able to manipulate the entire arm The manual functions are greatly reduced because of inability to get the hand where it is needed.

THE FOREARM

Anteriorly the muscles and tendons can be palpated The extent to which these can be outlined by the examiner depends on the absence of subcutaneous fat and the degree of development and contraction of the individual muscles The skin of the forearm is loose and thin. The median vein is situated on the flat surface; the radial vein winds around the back of the wrist and crosses the outer edge of the radius about its middle On the medial side near the elbow the anterior and posterior ulnar veins are visible as they pass posteriorly

On the posterior surface of the forearm the bones are more conspicuous than on the anterior surface because they are subcutaneous By palpation the ulna can be traced down the forearm, running from the olecranon process down to its styloid process at the back of the wrist To the outer side of the olecranon can be felt the lateral (external) epicondyle and the capitulum humeri If the elbow is extended, a dimple is seen just below the capitulum humeri, it marks the position of the head of the radius.

By placing the thumb of one hand in the dimple on the head of the radius, and *rotating the hand of the patient with the other, the examiner can feel rotation* of the bone and thus be assured that the radius is intact Whenever fracture of the radius is suspected, this is the procedure resorted to in order to determine whether or not the radius is broken

The radius can be followed distally only for a distance of about 1 inch (about 2 5 cm.), where it disappears beneath the muscles to become subcutaneous again on the lateral side of the middle of the forearm. Thence it can be palpated to the styloid process on the lateral side of the wrist

Movements of the Forearm. In the midposition, with the radius above the ulna, the space between the bones is at its maximum. It is this space which, if encroached on by poor apposition of fractured bones, results in limitation of movements of pronation and supination The head of the radius rotates in the orbicular ligament; the lower end of the radius revolves around the head of the ulna The range of movement is from 140 degrees to 160 degrees.

The muscles of supination are stronger than those of pronation, and it is for this reason that *instruments intended* to be used in a rotary manner are *designed to turn* from the inside toward the outside, that is, in the direction of supination (for ex-

situated in the hand itself An especial accomplishment of the human hand is the ability to oppose the thumb to the other digits

Movements. The motion between the individual carpal bones is limited to a slight gliding on one another. The summation of these motions, however, permits considerable range of movements. These movements are flexion and extension, abduction and adduction and circumduction. If motion is prevented in the bones of the forearm, it is impossible to rotate the hand.

The *radiocarpal joint* has a greater degree of flexion than of extension The movement permitted between the two rows of carpal bones is extensive

The movements of the four midcarpometacarpal joints are flexion (toward the palmar surface) and slight extension There is slight lateral flexion and extension which enables cupping of the hand for grasping round objects. The articulation of the thumb allows flexion, extension, abduction, adduction, and circumduction, but not rotation.

The *metacarpophalangeal articulations* of the fingers are practically saddle-shaped joints resembling somewhat the ball and socket joints with all their movements except that of rotation They can be flexed to an angle of 90 degrees The interphalangeal joints are hinge joints and capable only of flexion and extension The second joint can be flexed to an angle of 120 degrees and the end joint to about a right angle The prominence of the knuckle is formed by metacarpal bone.

Functional Testing of Muscles of the Arm and Hand. *Biceps.* The patient extends the arm and flexes it at the elbow. Further attempts of flexion are resisted by the examiner The muscle can be seen and felt (Fig 6-24). (Musculocutaneous nerve supply, C_5, C_6)

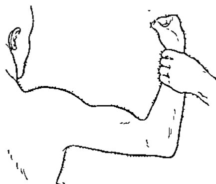


Fig. 6-24 Biceps muscle Standing or sitting with the arm extended laterally at the shoulder and supinated and flexed at the elbow Attempts are made to flex the supinated arm at the elbow The muscle can be seen and felt Nerve supply C_5, C_6 *(musculocutaneous nerve)*

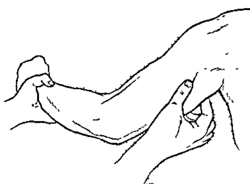


Fig 6-25. Triceps muscle Long heads Standing, sitting or lying so that the force of gravity is inoperative on the flexed arm at the elbow Attempts are made to extend the forearm against resistance The muscle can be seen and felt in either place shown Nerve supply C_7, C_8 *(radial nerve)*

Triceps The triceps may be tested as is the biceps, except that the previously flexed arm is to be extended against resistance. The muscle can be seen and felt The long heads of the triceps muscle can be palpated here (Fig 6-25) The whole or cross section of the triceps muscle can be palpated at the level of the arm indicated (Fig 6-26). (Radial nerve supply, C_7, C_8)

Brachioradialis. With the forearm midway between pronation and supination, the attempt at flexion renders the belly of the muscle evident (Fig 6-27). (Radial nerve supply, C_5, C_6)

Extensor Carpi Radialis Longus With the fingers extended, attempt is made to extend the wrist to the radial side The contracted muscle can be felt (Fig 6-28). (Radial nerve supply, C_6, C_7)

bones that adhesions from the coagula may become very extensive. Rheumatic fibrositis is recognized by persistent and painful stiffness. It is commoner in those past 40 years of age than in younger persons.

As the angle of extension is lost in the wrist, the flexion power of the fingers is diminished accordingly and the deformity becomes more disabling. The prominence of the base of the hand over which the flexor tendons pass increases the flexor tension as the hand is dorsiflexed. When the hand cannot be dorsiflexed to or past the 180 degree line, therefore, the long flexor tendons are at a disadvantage. Rigid fixation in flexion eliminates the action of all muscles of the wrist. The flexion power of the fingers is less when the fixed position is in abduction to the radial side than when in adduction to the ulnar side.

When the wrist is fixed in *dorsiflexion*, the palm of the hand is serviceable and the prominence of the base of the hand retains its function. The flexor action of the fingers approaches normal The degree of adduction decreases the strength of fingers, while abduction strengthens them. The thumb flexors are improved in strength in the position of ulnar flexion or adduction. In fixed ankylosis, therefore, midpronation is the position of choice.

When the limitation of rotation originates at the elbow, the biceps may be influenced through limitation of flexion.

In the ankylosed position of full supination the hand is turned the wrong way to be useful. As the range of motion approaches midway between pronation and supination, the fingers and hand increase in their usefulness but the most useful position is that of about 35 to 45 degrees of pronation (McBride)

THE HAND

Man alone has a hand All other mammals have paws or front feet With respect to length, the hand is classified as being long or midlong or short. With respect to breadth, the hand is spoken of as being broad, midbroad or narrow. Absolute breadth of the hand increases with age and is enhanced by physical labor in the early period of life, so that among middle-aged adults there are more than twice as many broad hands as all other widths combined

On the dorsum of the hand the extensor tendons can be seen Accessory slips usually connect the tendon of the ring finger with the tendons of the little finger and middle finger A slip also usually passes from the tendon of the middle finger to that of the index finger.

On the dorsum of the hand the metacarpal bones are subcutaneous and can be felt in their entire length The muscular prominence on the dorsum of the hand seen when the thumb and the forefinger are approximated is due to the abductor indicis muscle. At its upper extremity the radial artery passes between the two heads of the muscle to enter the palm When the thumb is extended, the *anatomist's snuffbox* becomes evident and the extensor pollicis longus tendon is distinctly seen leading to the ulnar side of the posterior radial (thecal) tubercle on the middle of the dorsum of the radius. The tendons on the radial side of the snuffbox are the extensor brevis and extensor ossis metacarpi pollicis.

If the hand is turned with the palm up, the thumb diverges from the median line at varying angles The palm is the hollow of the hand formed by a muscular mass on each side. On the thumb side is the *thenar eminence*, on the ulnar side is the *hypothenar eminence* The palm is marked by four creases, two longitudinal and two transverse, caused by flexions of the digits. Fortunetellers lay more stress on their "knowledge" of the importance of these creases than they deserve.

The fingers perform many complicated movements. The movements of the hand and fingers are accomplished by the action of the long flexors and extensor muscles of the fingers and the flexor and extensor muscles of the carpus, which arise in the forearm. Perfection of motion is added by the actions of numerous short muscles

Abductor Pollicis Longus. The patient tries to abduct the thumb in a plane at right angles to the palm. The tendon can be seen and felt (Fig. 6-32). (Radial nerve supply, C_7-C_8.)

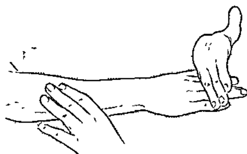


Fig 6-30 Extensor digitorum muscles. Forearm and hand resting on flat surface with the palm downward Attempts are made to flex the fingers against resistance Nerve supply C_7, C_8 (radial nerve)

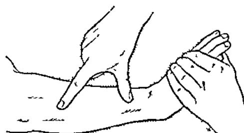


Fig. 6-31 Extensor carpi ulnaris muscle Flexor surface of the arm down on flat surface Attempts are made to extend the wrist joint to the ulnar side against resistance Nerve supply C_7, C_8 (radial nerve).

Extensor Pollicis Brevis. The patient resists an attempt to flex the thumb at the metacarpophalangeal joint The tendon can be seen and felt (Fig 6-33). (Radial nerve supply, C_7-C_8)

Extensor Pollicis Longus The patient resists an attempt to flex the thumb at the interphalangeal joint The tendon can be seen and felt (Fig 6-34). (Radial nerve supply, C_7-C_8)

Pronator Teres The patient extends the arm by the side and resists the examiner's attempt to supinate the hand The muscle belly can be felt and sometimes seen (Fig 6-35) (Median nerve supply, C_6-C_7.)

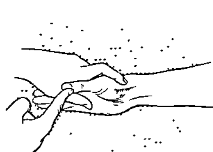


Fig 6-32 Abductor pollicis longus muscle Ulnar surface of arm flat on table Attempts are made to abduct the thumb in a plane at right angles to the palm The tendon can be felt and seen Nerve supply C_7, C_8 (radial nerve)

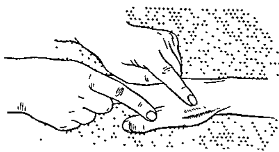


Fig 6-33 Extensor poll . . . [illegible] seen and felt Nerve supply C_7, C_8 (radial nerve)

Flexor Carpi Radialis The patient tries to flex the wrist toward the radial side against resistance The muscle belly can be felt and the tendon can be seen (Fig 6-36) (Median nerve supply, C_6, C_7, C_8)

Flexor Digitorum Sublimis. The patient resists an attempt to straighten any finger at first interphalangeal joint, while the proximal phalanx is fixed The con-

Supinator Brevis. The patient extends the arm by the side, and resists the examiner's attempt to pronate the hand (Fig. 6-29). (Radial nerve supply, C_5, C_6.)

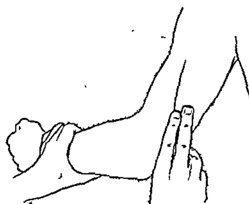


Fig 6-26 Triceps muscle The long heads or a cross section of the whole muscle can be palpated here when the patient tries to extend the arm against resistance (nerve supply C_7, C_8)

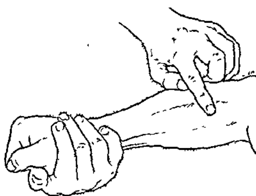


Fig 6-27 Brachioradialis muscle Arm flexed at the elbow while patient stands or sits The forearm midway between pronation and supination Nerve supply C_5, C_6 (radial nerve)

Extensor Digitorum Communis The patient resists an attempt to flex the fingers at the metacarpophalangeal joints. The muscle belly can be felt and sometimes seen (Fig 6-30). (Radial nerve supply, C_7, C_8)

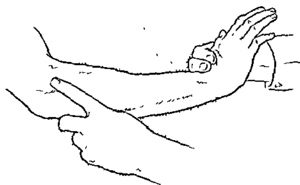


Fig. 6-28 Extensor carpi radialis longus Flexor surface of arm downward on flat surface Attempts are made to extend the wrist to the radial side against resistance The muscle can be felt Nerve supply C_6, C_7 (radial nerve).

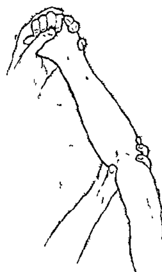


Fig 6-29 Supinator muscle Standing, lying or sitting with arm extended by the side Attempts are made to prevent the hand from being forcibly pronated Nerve supply C_5, C_6 (radial nerve)

Extensor Carpi Ulnaris. The patient tries to extend the wrist joint to the ulnar side against resistance The muscle belly can be felt and the tendon can be seen and felt (Fig 6-31). (Radial nerve supply, C_7-C_8)

Flexor Pollicis Longus The patient resists an attempt to extend the terminal phalanx of the thumb, while the proximal phalanx is fixed (Fig. 6-39). (Median nerve supply, C_8-T_1.)

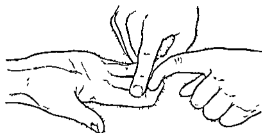


Fig 6-38 Flexor digitorum profundus muscle, I and II. Hand on firm surface, palm upward, the second phalanx is held in place, and attempts are made to extend the terminal phalanx of the index finger against resistance while the middle finger is fixed Nerve supply C_8, T_1 (median nerve)

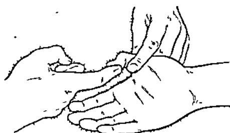


Fig 6-39 Flexor pollicis longus muscle Hand on firm surface, palm upward, the proximal phalanx is held by the examiner. Attempts are made to extend the terminal phalanx of the thumb against resistance while the proximal phalanx is fixed Nerve supply C_8, T_1 (median nerve).

Abductor Pollicis Brevis. The patient's thumb is placed so that the nail is in a plane at right angles to the palm of the hand, while supporting an object such as a pencil between the thumb and palm. The patient then tries against resistance to bring the edge of the thumb to a point vertically above its original position The thumb nail maintains its position in a plane at right angles to the palm (Fig 6-40). (Median nerve supply, C_8-T_1)

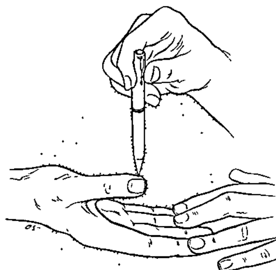


Fig 6-40 Abductor pollicis brevis muscle Hand on flat surface, palm upward, end of thumb over proximal palmar surface of index finger Attempts are made against resistance to bring the thumb to a position vertically above but proximal to the starting point while the thumbnail maintains its position in a plane at right angles to the palm Nerve supply C_8, T_1 (median nerve)

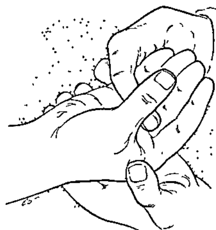


Fig 6-41 Opponens pollicis muscle The patient's arm at the elbow rests on firm surface with palm upward Attempts are made against resistance to touch the tip of the little finger with the thumb while the thumbnail remains parallel to plane of the palm The contraction of muscle is manifested by pressure exerted on examiner's right index finger. Nerve supply C_8, T_1 (median nerve).

vincing sign is the ability to flex the proximal joint while the terminal joint remains flaccid (Fig. 6-37). (Median nerve supply, C_7, C_8, T_1.)

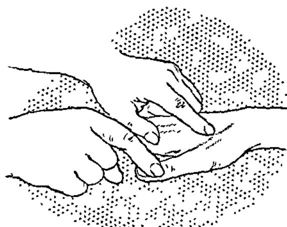


Fig 6-34. Extensor pollicis longus muscle Palmar surface of hand on flat firm surface Attempts to flex the thumb at the interphalangeal joint are resisted (Tendon can be seen and felt) Nerve supply C_7, C_8 (radial nerve)

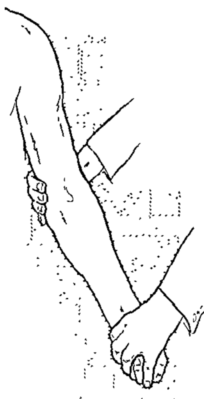


Fig 6-35 Pronator teres muscle Standing, sitting or lying with arm extended by side Attempts to supinate the hand are resisted The muscle can be felt Nerve supply C_6, C_7 (median nerve)

Flexor Digitorum Profundus I and II. The patient resists an attempt to extend the terminal phalanx of the index finger, while the second phalanx is fixed (Fig. 6-38) (Median nerve supply, C_8-T_1)

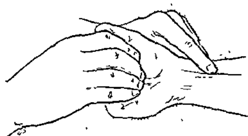


Fig 6-36 Flexor carpi radialis muscle Attempts are made to flex the wrist toward the radial side The muscle can be felt and seen. Nerve supply C_6, C_7, C_8 (median nerve).



Fig 6-37 Flexor digitorum sublimis muscle Hand on firm surface with palm upward, the proximal phalanx is fixed by pressure from the examiner's fingers. Attempts are made to straighten any finger at its first interphalangeal joint The proximal joint can be flexed while the distal joint remains flaccid. Nerve supply C_7, C_8, T_1 (median nerve).

flexor carpi ulnaris is intact, this movement is observed even when abductor digiti minimi is paralyzed. (Ulnar nerve supply, C_7-C_8.)

Flexor Digitorum Profundus III and IV. The patient resists an attempt to extend each finger in turn at the distal interphalangeal joint, while the middle phalanx is fixed (Fig. 6-45). (Ulnar nerve supply, C_8-T_1.)

Abductor Digiti Minimi. With the back of the hand and the fingers flat upon a table, the patient tries against resistance to abduct the little finger. The muscle belly can be felt (Fig. 6-46). (Ulnar nerve supply, C_8-T_1.)

First Dorsal Interosseous Muscle. With the fingers and palm flat upon a table, the patient tries against resistance to abduct the index finger. The muscle belly can be felt and usually seen (Fig. 6-47). (Ulnar nerve supply, C_8-T_1.)

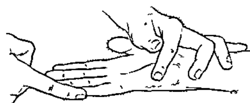


Fig. 6-46 Abductor digiti minimi muscle. Hand on firm surface, palm upward and held in place by the examiner. Attempts are made against resistance to abduct the little finger. The muscle can be seen and felt. Nerve supply C_8, T_1 (ulnar nerve).

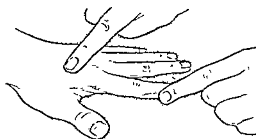


Fig. 6-47 First dorsal interosseous muscle. Hand on firm surface, palm downward and snugly applied. Attempts are made to abduct index finger against resistance. Nerve supply C_8, T_1 (ulnar nerve).

First Palmar Interosseous Muscle. With the fingers and palm flat upon a table, the patient tries against resistance to bring the abducted index finger toward the median line (Fig. 6-48). (Ulnar nerve supply, C_8-T_1.)

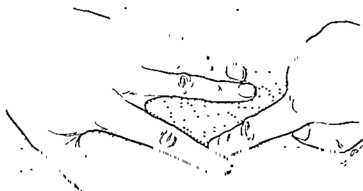


Fig. 6-48 First palmar interosseous muscle. Hand on firm surface, palm downward and snugly applied to the surface. Attempts are made against resistance to bring the abducted index finger back in place. Nerve supply C_8, T_1 (ulnar nerve).

Adductor Pollicis. With the thumb placed along the palmar aspect of the index finger, the patient tries against resistance to retain a piece of paper between the thumb and the palm (Fig. 6-49). (Ulnar nerve supply, C_8-T_1.)

Opponens Pollicis. The patient tries against resistance to touch the tip of the little finger with the thumb, while the thumb nail remains in a plane parallel to the palm (Fig. 6-41). (Median nerve supply, C_8-T_1.)

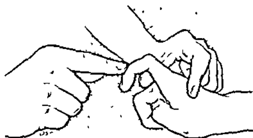


Fig. 6-42 Lumbrical-interosseous muscle of index finger Arm with palmar surface downward on firm base, hand held by examiner while the first metacarpophalangeal joint is hyperextended and fixed Attempts are made to extend the first interphalangeal joint against resistance The muscle can be seen and felt Nerve supply C_8, T_1 (both median and ulnar nerves)



Fig 6-43 Flexor carpi ulnaris muscle Hand with fingers extended, palmar surface *upward, on flat firm surface* Examiner's hand in place indicating extent of muscle Nerve supply C_7, C_8 (ulnar nerve)

Lumbrical-Interosseous Muscle (Index Finger). With the metacarpophalangeal joint hyperextended and fixed, the patient tries to extend the first interphalangeal joint against resistance. The belly of the first dorsal interosseous muscle can be seen and felt (Fig. 6-42). (Median and ulnar nerves, C_8-T_1.)



Fig. 6-44 Flexor carpi ulnaris muscle (little finger) Hand resting and fixed on firm surface, palmar surface upward, fingers extended Attempts are made to abduct the little finger The tendon can be seen and felt Nerve supply C_7, C_8 *(ulnar nerve).*

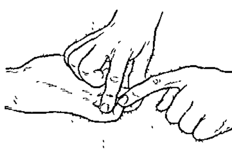


Fig 6-45 Flexor digitorum profundus III and IV of fingers Both fingers are tested as illustrated for little finger, While the middle phalanx is fixed on a firm flat surface attempts are made against resistance to extend the finger at the distal interphalangeal joint while its middle phalanx is fixed The strength of the flexors can be determined by the examiner's fingers Nerve supply C_8, T_1 (ulnar nerve).

Flexor Carpi Ulnaris. The patient lays the hand palm upward on the table, the fingers being extended (Fig 6-43). The patient then tries to abduct *the little finger* fully (Fig 6-44). The tendon of flexor carpi ulnaris can be seen and *felt* as the muscle comes into action to fix the point of origin of abductor digiti minimi. When

reddened. The uniformly reddened skin is the characteristic appearance. In mild cases only the eminences of the palms and fingers are affected. The color blanches on pressure with a more rapid return of the color than in the normal hand Fading of the color does not take place on elevation Definite flushing synchronous with pulse is observed when the color is partially obliterated with a glass slide.

On direct microscopic examination the capillaries are said to be more numerous and dilated than normally. Palmar erythema is often associated with vascular spiders.

Handedness and Its Associations. Handedness may be defined as the preferential use of either hand Most persons are right-handed A few are left-handed, and some have preferences for use of the hands which are different for different tasks

There seem to be varying degrees of left-handedness, but only an extremely left-handed person differs so greatly in motor activity from right-handed persons in a right-handed environment that he is set apart and is immediately recognized as such. The left-handed person is compelled to adapt and to adjust himself to a right-handed environment In most instances the process of adjustment and adaptation is so successful that not even the affected person is conscious of a left-sided tendency Consequently, special tests must be used in order to recognize this peculiarity with certainty Card shuffling is a very good test for evidences of handedness

Generally, total left-handedness must be regarded as exceptional It is observed, however, that this small percentage of left-handed or exceptional persons have more than their share of speech disturbances (see Stuttering, Chapter 15), epilepsy, and moral and physical defects

There are differences in the right and left sides of the body incident to or associated with handedness The right and the left halves of the face differ from each other and present varying degrees of asymmetry Wolff concluded that the right half of the face bears the individual expression which the person exhibits in daily life, it presents those character traits and features which the person desires to portray In contrast to this, the left half of the face bears the person's extra expression, representing the hidden character traits which arise in the subconscious The right half of the face in right-handed persons is directed by the left hemisphere, which represents the seat of all rational conscious processes. The right cerebral hemisphere, about the importance of which very little is known, controls the left half of the face, the half which bears the expression of the subconscious

In the absence of any means of orientation both men and animals move in circular paths *This trait of circumambulation is termed the turning tendency.* The turning tendency in humans is associated with handedness Right-handed persons turn chiefly toward the right, and left-handed ones to the left. This trait becomes apparent when a right-handed and a left-handed person are together and are lost in the woods The right-hander wishes to go to the right and the left-hander to the left and thus an argument ensues

The natural turning tendency in either man or animal is lost when the individual is wounded The path, after the person or animal is wounded—shot—is straight away from the scene of the tragedy

Regarding the postural and motor acts which are peculiar to man and which consist in interaction of two extremities, some individuals will favor one side and others will reveal no preference for either side, and thus these acts cannot be associated with handedness However, the manner in which a person folds the hands and crosses the arms rather specifically indicates handedness. For example, the superposition of the left thumb upon the right when the hands are folded is an indication of left-handedness

The foot which is passed forward to test the strength of ice or the softness of the ground before treading on it is an indication of footedness It may be observed that the footedness is contralateral to the handedness. For instance, a right-handed

Opponens Digiti Minimi. Fingers extended, the patient tries to make a cup of the palm and to carry the fifth finger in front of the others (Fig. 6-50). (Ulnar nerve supply, C_8-T_1) *

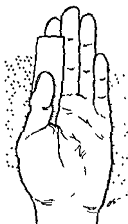


Fig 6-49 Abductor pollicis muscle Hand on firm surface, palm upward, fingers extended, thumbnail in a plane at right angles to the palm Ability to hold a piece of paper against resistance indicates intact muscle. Nerve supply C_8, T_1 (ulnar nerve)

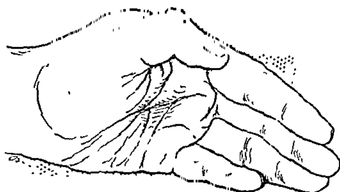


Fig 6-50 Opponens digiti minimi muscle The ulnar aspect of the arm rests on flat surface with thumb upward Attempts are made to form a cup of the palm while carrying the little finger in front of the others Nerve supply C_8, T_1 (ulnar nerve)

The Palmar Fascia. The palmar fascia or aponeurosis is the deep fascia of the hand It consists of a thick triangular middle portion and two thin lateral portions which cover the thenar and hypothenar eminences. This fascia is often involved in injuries and infections of the hand Dupuytren's contracture is a congenital anomaly involving the fascia of the hand (see Disease of Fascia, p 273).

Palmar Erythema. The palmar surface of the hand is less pigmented than is the dorsal surface. In the absence of callus, the lividity of the palmar and dorsal surfaces of the hand is equal A morbid redness of the skin of the palmar surface is palmar erythema, a condition due to dilatation of the capillaries in the pads of the palm and fingers The covering skin is normal

Palmar erythema on rare occasions may be present in an otherwise normal person. It is usually associated with some sort of chronic illness and often an illness in which there is an associated hypoalbuminemia. It may be present in liver disease and during the last trimester of pregnancy. However, it may be associated with chronic diseases of many kinds

Palmar erythema occurs in both men and women There are no symptoms. However, the patient may be concerned about the appearance of the hands.

Examination reveals symmetrically reddened eminences of the pads of the terminal digits, the palms and sometimes the soles of the feet. The transverse creases of the fingers may be of a deeper color than the adjacent skin The redness may extend over the finger tips to the nail beds and laterally over the distal phalanges. The color may be a diffusely mottled redness, small telangiectatic spots or uniformly

* Acknowledgment is made to the Controller of Her Britannic Majesty's Stationery Office for permission to make line drawings of photographs of muscles in action in War Memorandum No 7, reprinted 1945.

Of the *chronic inflammations* in and about the *wrist*, chronic infectious arthritis is very common. If one wrist alone is affected, and no other joints in the body are involved, tuberculosis of the joint is probable. It is easily distinguishable from tuberculous tenosynovitis, since in the latter the swelling is only on one side of the wrist, usually the volar side, and is most marked, not at the level of the wrist itself, but proximal and distal therefrom. The fingers are slightly flexed and there is no volar subluxation of the hand as in tuberculous arthritis

Of the chronic inflammations of the *hand* and *fingers*, the common ones are (1) tuberculosis of the tendon sheaths, especially of the flexor tendons, (2) gonorrheal tenosynovitis, (3) the stenosing tenosynovitis (radiating pain in the thumb and forearm on use), due to stenosis of the compartment of the tendon sheath for the extensor hallucis brevis muscle and the abductor hallucis longus muscle over the styloid process of the radius and (4) the spindle-shaped swellings of the metacarpal bones or phalanges, due to tuberculosis or to syphilis

Tenosynovitis (*Perimyotendinitis*). Traumatic tenosynovitis is distinct from pyogenic or granulomatous involvement of the tendon sheaths. The term tenosynovitis applied to the usual crepitating condition found proximal to the wrist joint is a misnomer The actual site of the lesion is well above the upper limit of the tendon sheaths at the wrist.

The local manifestations suggest that the lesion is essentially a perimyotendinitis involving the more proximal musculotendinous junction in the forearm It affects mostly factory workers, agricultural workers and housewives The tendons most frequently affected are the radial extensors of the wrist (extensor carpi radialis longus and brevis) and the abductor pollicis longus or extensor pollicis brevis, either alone or in combination The main factors in the etiology are unaccustomed movement, resumption of work after absence, repetitive stereotyped movement and local strain The prognosis is good, and cessation of work is neither desirable nor necessary.

Neoplasms. The wrists are rarely affected by neoplasms. The commonest tumors of the wrist are the osteophytic outgrowths from the bases of the distal phalanges in certain elderly persons The wrist joint may be affected by sarcoid and giant cell tumors

Diseases Due to Trauma or Physical Agent. ***Abscesses of the Hand and Fingers.*** Purulent collections in the palm of the hand either are situated beneath the palmar fascia or are connected with the sheaths of the flexor tendons

When pus collects beneath the palmar fascia, it is limited in the directions in which it can spread Pus originating beneath the thick middle triangular portion of the fascia may point in one or more of several places (1) on the inner side at the hypothenar eminence, (2) in the web of the thumb, (3) on the anterior surface of the forearm above the wrist and (4) on the webs of the fingers. Also in rare instances (5) it may burrow between the distal extremities of the metacarpal bones and show on the back of the hand and (6) if there should be, as is sometimes the case, tiny gaps in the fascia, a small amount of pus may accumulate above the palmar fascia and between it and the skin, so that there is a collection of pus both above and below the fascia

If the sheaths of the tendons of the hand or fingers become infected, the pus passes along the tendon as far as the sheath extends Since the extent of the tendon sheaths varies, it is well to recall that when suppuration occurs in the sheath of the thumb or little finger it is much more serious than in the other three, because the pus tends to pass directly upward, involve the palm and extend to the arm When suppuration involves the index, middle or ring finger, it stops when it reaches the vicinity of the metacarpophalangeal joints and involves the palm only. It may penetrate the carpal bursa

When the end phalanx becomes infected, the affection is known as a *felon* The

person may twist and prefer use of the left foot for purposes of exploration of the safety of the terrain for walking but will kick a football with the right foot.

Abnormalities of the Hand. The *spade hand*, large, coarse, thick-fingered, with broad nails, is seen as an evidence of myxedema, in which the enlargement affects mainly the soft parts; and in acromegaly, in which the enlargement affects the bones

The *clawhand*, also called *main en griffe* (griffin hand), is a deformity which occurs in consequence of paralysis and atrophy of the interossei and lumbricales muscles Paralysis of these muscles leads to a dorsal extension of the proximal phalanges with flexion of the others, and when atrophy takes place, the clawhand results. This abnormality suggests the existence of a neuritis of the median and ulnar nerves, particularly the latter, or progressive muscular atrophy. Similar deformities may be due to amyotrophic lateral sclerosis (the spastic form of progressive muscular atrophy), syringomyelia and, very rarely, the adult type of chronic anterior poliomyelitis

Atrophy of the muscles of the hand and forearm occurs in brachial palsies, but also to a slighter degree in cerebral paralysis in consequence of disuse and lower motor neuron lesions

Coldness of the hands and feet, with or without a tendency to sweating, if persisting for weeks or months, is most commonly due to neurasthenic conditions. Sudden or transient coldness of the extremities is observed in many persons, especially those of a nervous temperament, under excitement or anxiety, as well as in shock, collapse, hemorrhages and premonitory chilliness of rising fever. Coldness of the hands is also observed in Raynaud's disease and Buerger's disease It is necessary to discriminate between actual lowering of the temperature palpable to the observer and a subjective sensation of coldness The latter is a paresthesia

Excessive *sweating of the hands* may be due to nervous tension, toxic goiter and, occasionally, progressive muscular atrophy

In determining the existence of enlarged joints, it must not be forgotten that atrophy or wasting of the soft parts may cause an apparent increase in the size of the joints

Diseases of the Wrist and Hand. The more distinctly medical diseases of the wrist and hand include the inflammations, the neoplasms and trauma

Inflammations of the Wrist and Carpal Region. The *acute inflammations* of the wrist joint and its neighborhood (chirarthritis) are (1) acute arthritis of the wrist due to acute rheumatic fever or other forms of acute infectious arthritis and (2) acute inflammation of the vaginae mucosae (tenosynovitis) secondary to a penetrating wound of a finger, to a bite (human or animal) or other injury, or, sometimes, to metastatic infection

In tenosynovitis it is chiefly the movement of the fingers that is disturbed, whereas in arthritis of the wrist it is chiefly movements of the hand as a whole that are concerned, moreover, in arthritis there is everywhere about the affected joint tenderness on pressure, while in tenosynovitis only the side affected is tender Again, traction or compression in the long axis of the extremity is painful in arthritis, not in tenosynovitis. Extension of the inflammatory process in the longitudinal direction is characteristic of tenosynovitis, in arthritis, the inflammation remains limited to the joint region Sometimes, of course, arthritis and tenosynovitis occur together.

A painful swelling in the region of the long extensor of the thumb, accompanied by crackling on palpation over the tendon and muscle, is the so-called tenosynovitis crepitans; it is a chronic inflammation of the vaginae mucosae of the tendon and of the surrounding tissues

[illegible] The proximal [illegible] onic infectious

Eczema of the Hands. Eczema of the hands may be self-limited, as in occupational eczema of the hands in which the skin becomes hardened, or it may be a permanent state in which remissions and exacerbations alternate. A familial history of eczema or a history of infantile eczema is significant, because it indicates an allergic state.

There are many known causes for eczema of the hands and probably just as many unknown causes The known causes are fungous infections and their reactions, occupational irritants, dietary factors, neurodermatitis, dyshidrosis (pompholyx) and drug eruptions. The presence of an acute vesicular eruption indicates that the skin is hypersensitized and is prone to react unfavorably to therapeutic agents that are not mild and soothing

Eczema or dermatitis of the hands consists of a vesicular or scaling, oozing or weeping, crusted or infected eruption of the hands In the acute phase it is characterized primarily by vesicles and erythema, when subacute, by scaling and erythema, and in the chronic phase, by thickening or lichenification and scaling.

Diseases of the Nails. ***Congenital Abnormalities.*** Congenital absence of the nails (anonychia) is very rare It may be associated with congenital ichthyosis; if so, nails may or may not appear later in life

The presence of extremely small, otherwise apparently normal, nails is termed micronychia Extremely large nails (macronychia) appear as a congenital abnormality; they also develop later in life in the course of acromegaly or macrodactylia and may, at times, be associated with clubbing of the fingers

Pachyonychia is a congenitally thickened and discolored nail which may also be abnormally hard and longitudinally striated

Nails may be present in abnormal situations, for instance, on the palmar surface of a finger or the plantar surface of a toe This condition is known as onychoheterotopia.

Infections. Tuberculosis, anthrax, leprosy, virus of verruca vulgaris, syphilis, and mites of scabies may cause nail changes Most cases of suppurative paronychia, however, are caused by staphylococci, whereas nonsuppurative paronychia often results from moniliasis

Syphilis affects the nails in a variety of ways. However, these changes are not constant or definite. The diagnosis of syphilis is made on the presence of positive serologic reactions which are associated with other evidence of syphilis elsewhere in the body. If all of these findings are present and there is no evidence for any other causative disease, the changes in the nails may be attributed to syphilis

Fungous disease or "ringworm" of the nails—onychomycosis—causes severe disturbances of nail growth and local destruction of the nails of the toes or fingers Nail foci may provide sources of infection or reinfection to the glabrous skin The abnormalities of nail structure may be so severe as to be incapacitating, as in mycotic onychauxis and onychogryposis

The fungi causing the different types of onychomycosis are many and varied: Trichophyton, Epidermophyton, *Candida albicans* (*monilia*), Penicillium, Aspergillus (see Diseases of the Skin, Chapter 8)

When a nonsuppurative paronychia is present, moniliasis caused by *Candida albicans* is to be suspected, especially in fruit pickers and handlers, dishwashers, housewives, dentists and others whose nails are wet during prolonged periods.

Because of the close resemblance of onychomycosis to psoriasis, the diagnosis always depends on microscopic and cultural identification of the fungi. Positive cultures are obtained from 1 of every 5 who have the disease.

Trauma. Schwartz, Tulipan and Peck have considered in detail the effects of trauma to the nails Hemorrhage beneath the nail plate (subungual hematoma) may be caused by a bruise, and the nail may subsequently be loosened and fall away. Deep splinters may cause longitudinal white streaks, a form of leukonychia. Spoon-shaped nails (without regrowth) may form; or in elderly patients such a nail may

skin over the pad of the finger sends off fibrous bands or fibrils which are attached to the parts beneath. An infection of the skin can pass through it and involve the fatty tissue beneath. The pus is often unable to break through the skin. Since the fibrous bands prevent swelling, it burrows and involves the periosteum and thence to the region of the joint, where it may enter the sheath. Once the pus is within the tendon sheath it extends as far as the sheath goes

In pursuit of his labors, man is exposed to various hazards that deform his body and cripple his hands The changes which affect the hand under the influence of mechanical, chemical, thermal, electric and atmospheric stimuli are numerous. These changes may be characteristic of certain trades, so that they may be regarded as trade stigmas For instance, hands which are in constant contact with water may be affected by an alteration of the skin, characterized by softening, chapping and often ulceration, with veritable destruction of the parts.

The trade stigmas of the hands have been classified by various outlines. Oppenheim, long ago, enumerated these stigmas as stains or coloring A more recent classification has been enumerated by Schwartz, Tulipan and Peck as: stratifications, excoriations, telangiectases, nail changes, pigmentation, callosities, bursae, cicatrices and tattooing

The nails frequently exhibit trade stigmas. The right thumbnail in women who remove the indigo fruit from its shell is long In watchmakers and clockmakers this nail is short The nails of laundresses and lens grinders are short and cracked

The hands become covered with particles of the material used at the place of work. Thus deposits of coal dust forming indelible blue-black scars enable one to recognize the coal miner who, when working, soils every scratch with coal dust. Similar deposits in the skin are found among metal workers, millers, and stonemasons

Superficial wounds, excoriations and rhagades are to be found among seamstresses, dressmakers, cobblers and glassworkers. The hands of glassblowers commonly exhibit wheals, flat plaques, rhagades and warts. (For further discussion of trade stigmas and mutilating affections of the hands, see Chapter 24)

Ankylosis of the Hand. The finger and wrist flexors are stronger than the extensors. The adductors of the thumb are stronger than the abductors. The wrist or fingers stiffen in a flexed position, or the thumb in an adduction deformity when prevented from use

Prolonged immobilization is probably the most frequent cause of stiffness in the hand, because of the necessity of continuous splinting in injuries of the arm or the hand In nerve injuries, in loss of substance, and in suppurations such as palmar abscess, the usefulness of the hand is sometimes totally lost Without the use of the hand grasp, all the wide excursions of the elbow and shoulder are useless Impediment in the shoulder or the elbow also limits use of the hand.

A *snapping finger* is produced by some obstruction to the action of the long dorsiflexor tendons under the ligament across the joint If painful or disabling, determination of the nature of the obstruction is made.

Ankylosis or Loss of the Thumb. Without use of the thumb the hand is left with only parallel digits, and the palm is the only opposing force in the act of gripping.

The fingers bear the evidence of the influence of the cerebral cortex on the acquisition of willed movements. They possess the tactile senses so necessary for the most technical accomplishments of the hand or the coarser squeezing duties which require strength and action. Without the fingers or thumb the hand becomes useless. Without individual action the finer functions of the fingers are lost. Therefore the interruption of perfection in one digit disturbs the synchronization and proficiency of the entire hand.

Nutritional Deficiency. Egg-shell nail is commonly seen in avitaminosis A Koilonychia (spoon nails) may be present in association with dysphagia, glossitis and [illegible] ise. Beau's [illegible] malnutri-

Changes in Dermatoses. LICHEN PILARIS SEU SPINULOSUS In lichen pilaris (keratosis pilaris) atypical nail changes may occur.

KERATOSIS FOLLICULARIS (DARIER'S DISEASE). The nails may become friable and split, and onychauxis, onychogryposis, paronychia and longitudinal ridges may develop

EXFOLIATIVE DERMATITIS Onychomadesis is of frequent occurrence in exfoliative dermatitis, as in drug sensitivity However, regrowth often takes place.

ALOPECIA AREATA In alopecia areata interruption of nail growth producing Beau's lines, thinning, and increased friability may be present. Regrowth almost invariably occurs.

ECZEMA. Nail changes in eczema are highly varied, ranging from minor disturbances of growth and distortion of structure to almost complete erosion and onychomadesis. Suppurative paronychia is frequently associated with eczema.

Nail changes occasionally occur in psoriasis.

Tumors Involving the Nails. Nails can be deformed in varying degrees by verruca, clavus, and exostoses of the phalanges A chondroma in the terminal phalanx causes deformation of the nail A glomus tumor may arise immediately beneath the nail bed, on which it may encroach, to become visible as a bluish discoloration under the nail plate A glomus tumor is exquisitely painful A simple angioma may be observable as a red discoloration in the nail bed or about the nail Occasionally, a melanoma originates from the matrix or nail fold. A fibroma may be observed beneath the nail bed or about the nail

DISEASES AFFECTING THE ARM AND HAND AS A WHOLE

Arachnodactyly. The individual afflicted with arachnodactyly according to Parker and Hare is tall, with excessively long arms and legs, long, thin, spider-like hands, meager subcutaneous fat, under-developed, atonic musculature and often ectopia lentis The emaciation accentuates the bony landmarks, and these in turn serve to emphasize the disproportionate length of the extremities as compared to the trunk The delicately elongated, spider-like fingers give this syndrome its name. The feet and toes are likewise long and slender Deformities of the joints are common Pes planus, contractures, hammer toes, webbing and sometimes abnormally mobile patellas occur The frequently associated scoliosis, kyphosis, winged scapula and deformities of the sternum are considered to be the result of the laxity of the ligaments and atonic musculature. The skull of the arachnodactylic patient tends to be dolichocephalic with prominent supra-orbital ridges, frontal bossing, a pointed chin and either a prominent or a broad, somewhat flattened nose The face is usually drawn, wrinkled and old looking, often with a melancholy expression. The ears are frequently enlarged Approximately 50 per cent of the patients have a partial dislocation of the lens, usually upward Congenital heart anomalies frequently accompany the disease and consist mainly of a patent foramen ovale and other interauricular septal defects In the infant or rapidly growing child this syndrome may resemble rickets The abnormally long and slender extremities, the absence of flared epiphyses, normal blood calcium and phosphorus, and perhaps obscure anomalies in the parents, should lead one to suspect arachnodactyly The symptoms of weakness, fatigue, moderate dyspnea on exertion, malnutrition and a coarse systolic murmur in early childhood may focus attention on the cardiovascular system to the exclusion of what appear to be lesser anomalies. This syndrome is not considered to be of endocrine origin

Venous Obstruction in Upper Extremity. An arm of an otherwise healthy person may become diffusely swollen and discolored. It has been suggested that

become wrinkled, and hyperkeratosis of the periungual tissues may form and malignant degeneration with the formation of epithelioma may ensue

Chemical Agents There are a number of chemical agents, among which are included soap, nail polish, polish remover, nail polish undercoats, dyes and industrial chemicals, which injure the nails Pigmentation or discoloration of the nail may be produced by contact with *topical medicaments* such as gentian violet, mercurochrome, silver nitrate, chrysarobin, silver-containing compounds, arsenic, tobacco, and many chemicals used in industry However, in industry the offending substances are known and the hands are usually protected

Soaps, nail polish bases (undercoat), fabric fibers (wool, silk) and chemicals cause allergic lesions after repeated contact The lesions vary from leukonychia and minor ridging to marked destruction of the nail plate and inflammation of periungual and subungual tissues Often these lesions resemble those of mycotic infections and psoriasis

Nail discoloration and dystrophy may be due to nail polish and nail polish bases or undercoats Sulzberger and others have observed the clinical features associated with allergic eczematous reactions of the nail bed due to synthetic resin-rubber undercoats and they have enumerated the following features: (1) a discoloration, diffuse or punctate, of the distal portion of the nail which ranges from yellow through blue to black; (2) separation of the distal portion of the nail from its bed (onycholysis); (3) subungual hyperkeratosis, (4) erythema, edema and scaling of the fingertips under the free edge of the nail, and subjective symptoms in the areas, may occur if the nail which has an undercoat is subjected to repeated trauma

Nail discolorations occur as the result of injury to the tips of the fingers. The nails become separated from their beds—a condition known as onycholysis. Nails may become discolored and may separate if repeatedly subjected to external heat A splinter of wood, glass or metal often tears the nail away from its bed and causes discoloration and perhaps separation

Trauma and Physical Agents. Workers who use power-driven drills or hammers are subject to development of hyperkeratoses beneath the nails Gardeners, laborers, textile workers, and those who handle wool often suffer from nail infections following trauma (Schwartz, Tulipan and Peck have considered in detail diseases of the nails in industry)

[illegible] the first observable [illegible]e [illegible]h

as those of phosphorus and iodine

Enumeration of the early disturbances of nail growth caused by irradiation according to Schwartz are (1) thinning, softening and increased friability of the nail, (2) longitudinal splitting, (3) discoloration and (4) varying degrees of atrophy. As time passes after irradiation, transverse ridging (Beau's lines) and loss of the nail occur.

Vascular Disease. In both vasospastic and obliterative vascular disease the nails undergo specific changes indicative of the lack of adequate circulation.

In vasospastic conditions, according to Allen, a pterygium develops (1) the nail fold becomes thinner and the cuticle widens; (2) the normally distinct boundary between nail fold and cuticle, as well as that between cuticle and nail plate, is lost.

Pterygium is a common condition of the last two toe nails of apparently normal individuals It is also common, however, in Raynaud's disease and scleroderma. [illegible] the nail plate The [illegible], thick, rough, dark [illegible]al nerve lesions, as [illegible]

limb against resistance. The muscle bellies can be felt and sometimes seen (Fig. 6-56B).* (Superior gluteal nerve supply, L_4, L_5, S_1.)

The Hip Joint and Monarticular Disorders. The hip joint is a ball and socket joint. The functions of the hip are mobility and support. For the necessary support and limitation of extent of movements of the hip, there are strong bandlike ligaments uniting



Fig. 6-54 Adductor muscles of leg Lying on back with leg extended and abducted, patient attempts to adduct the leg against resistance The muscles can be seen and felt Nerve supply L_2, L_3, L_4 (obturator nerve)

the bones. In the upright position the center of the weight of the body falls in front of the axis of rotation of the hip joint When a person falls it is usually forward. Falls in any other direction are indicative of complete loss of balance

The head of the femur is 2 inches (about 5 cm) in diameter and spherical in shape. The acetabulum is deep The joint is airtight, and the femur is held in place by suction and ligaments

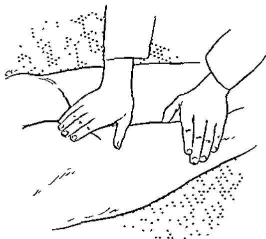


Fig 6-55 Gluteus maximus muscle Lying with face downward, abdomen and leg flat on firm surface, patient attempts against resistance to lift knee upward. The muscle can be seen and felt Nerve supply L_4, L_5, S_1, S_2 (inferior gluteal nerve)

The great pressure to which the articulating surfaces of the hip joint are subjected requires special lubrication of these surfaces, and this is supposed to be furnished by the ligamentum teres and haversian glands

Congenital Malformations of the Hip. In the anamnesis a history of limping or of waddling from earliest childhood can be obtained.

DISLOCATIONS. Congenital luxations, or dislocations, of the hip are most frequently posterior in position and are characterized by excessive mobility of the thigh. The manifestations of this deformity are no eversion, no flexion on lying down, and usually a high grade of lumbar lordosis on standing The acetabulum may be shallow. The head of the femur is deformed, and it occasionally is superior, but

* Acknowledgment is made to the Controller of Her Britannic Majesty's Stationery Office for permission to make line drawings of photographs of muscles in action in War Memorandum No 7, reprinted 1945

Sartorius. The patient lies on the back with the hip laterally rotated and tries to flex the knee against resistance. The muscle belly can be felt and sometimes seen (Fig 6-52). (Femoral nerve supply, L_2, L_3.)

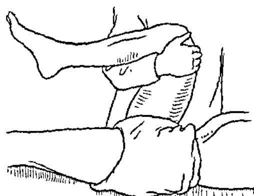


Fig 6-51 Iliopsoas muscle. Lying on back with the knee flexed, while the leg is supported at less than a right angle between the thigh and trunk Patient attempts to flex the hip against resistance Nerve supply L_1, L_2, L_3 (femoral nerve)

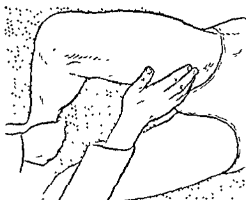


Fig 6-52 Sartorius muscle Lying on back with leg to be tested laterally rotated at the hip patient attempts to flex the knee against resistance Nerve supply L_2, L_3 (femoral nerve)

Quadriceps Femoris The patient tries to extend the knee against resistance The muscle bellies can be felt and often seen (Fig 6-53) (Femoral nerve supply, L_2, L_3, L_4.)

Adductors The patient lies on the back with the knee extended and tries to adduct the leg against resistance The muscle bellies can be felt (Fig 6-54). (Obturator nerve supply, L_2, L_3, L_4)

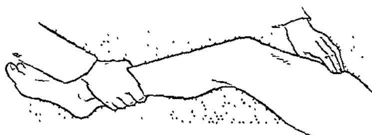


Fig 6-53 Quadriceps femoris muscle Lying on back with knee flexed, patient attempts to extend the knee against resistance The muscle can be seen and felt Nerve supply L_2, L_3, L_4 (femoral nerve).

Gluteus Maximus. In the prone position the patient tries against resistance to lift the knee. The muscle belly can be felt and often seen (Fig. 6-55) (Inferior gluteal nerve supply, L_4, L_5, S_1 and S_2)

Gluteus Medius and Minimus and Tensor Fasciae Latae (Rotation). To test internal rotation at the hip joint, the patient is in the prone position with the knee flexed to a right angle, and tries to carry the foot laterally against resistance. The muscle bellies can be felt and sometimes seen (Fig 6-56A). (Superior gluteal nerve supply, L_4, L_5, S_1.)

Gluteus Medius and Minimus and Tensor Fasciae Latae (Abduction). To test abduction, the patient lies on the back with the leg extended and tries to abduct the

Coxa vara is to be distinguished from (1) congenital dislocation of the hip, (2) beginning coxitis and (3) the effects of trauma.

Infections of the Hip Joint. Hip disease, coxitis or coxalgia in its early stage is characterized by pain, limitation of motion and limping The pain may be limited to the hip itself or referred. The hip is supplied by branches of the anterior crural, sciatic and obturator nerves, and since these also supply the region of the knee, disease of the hip often causes pain to be referred to the region around the knee joint.

In an early stage the limitation of motion is due to muscular contraction The limb is held in a position of flexion, abduction and slight external rotation. In mild cases the limitation is present as a reduction only in the normal extent of movements The abnormal changes are recognized by inspection, measurements, and comparison with the opposite healthy limb.

On inspection from behind, the gluteal fold is small over the affected side and the buttock is flattened The flattening of the buttock is caused by the flexion of the hip. An inequality in the lower limbs, whether due to shortening or to malposition, such as flexion, will be visible at once by an inequality of the gluteal folds, one being higher than the other. Flexion deformity is recognized, when the patient is standing, by the bending at the hip joint and by the lordosis or hollowing of the back. In flexion deformity of the hip, when recognized, the degree can be measured while the patient is in the recumbent position by the difference in the length of the legs.

The patient being flat on the back, the pelvis is made level by seeing that a line joining the two anterior iliac spines is at right angles to the median line. If abduction is present, the limb points away from the median line It cannot be brought straight down parallel with the sound leg without tilting the pelvis If measured from the umbilicus to the internal malleolus, the affected leg measures more than the sound one. This is called apparent lengthening. If when both limbs are placed in the same degree of abduction and are measured from the anterior iliac spine to the internal malleolus they measure the same, there is no real shortening.

In advanced disease, adduction is commoner than abduction. Adduction produces an apparent shortening, as shown by measurement from the umbilicus to the internal malleolus; if the sound limb is placed in the same degree of adduction as the infected one, the distances from the anterior iliac spines will show no actual shortening unless there is a loss of bone or displacement at the hip joint The pelvis, instead of being tilted down on the diseased side, is tilted up Flexion is usually more marked and the foot is usually inverted instead of everted.

In the diagnosis of the acute inflammations of the hip and its neighborhood, it is necessary to distinguish acute inflammations of the hip joint itself from osteomyelitis of the shaft of the femur. In the latter, cautious passive movement of the hip is possible and there is local tenderness below the trochanter. Also to be distinguished are iliac abscess, femoral or inguinal lymphadenitis and acute phlebitis of the femoral vein

If acute arthritis is present, it may be due to acute rheumatic fever, to other kinds of infectious arthritis, to syphilitic arthritis or to very acute tuberculous coxitis

CHRONIC COXITIS Of the chronic infections of the hip joint in childhood, by far the most important is tuberculous coxitis, the common hip-joint disease of childhood In adults nontuberculous arthritis is commoner including avascular necrosis

In *tuberculous coxitis* the child begins to show a painful limp, the gluteal fold disappears, and the muscles of the thigh begin to atrophy. Sometimes the child complains of pain in the knee rather than in the hip, but examination of the knee joint does not reveal anything abnormal there. On examination of the child lying on its

usually posterior, to the acetabulum. It can be moved backward and forward on the pelvis. The neck of the femur is twisted on its shaft.

There is shortening of the leg on the affected side when measurement is made from the anterior superior iliac spine The anterior iliotrochanteric angle is diminished or lost The tip of the trochanter lies abnormally high, above the Roser-Nélaton line. By palpation it can be recognized that the head is not in its normal position beneath the femoral artery. The superior border of the trochanter is on a level with the anterior superior iliac spine. Roentgenologic examination is necessary to ascertain accurately the position of the head and whether or not the bones possess their normal shape

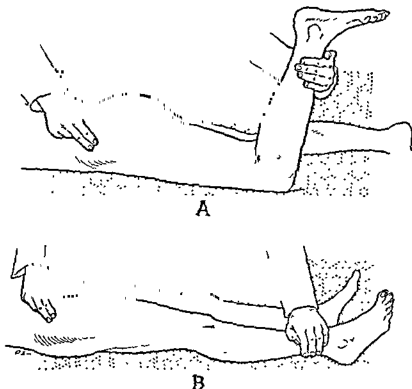


Fig. 6-56 A, gluteus medius and minimus and tensor fasciae latae muscles as internal rotators Lying with face downward, belly flat, leg flexed at knee, patient attempts to carry the foot laterally against resistance The muscle can be felt Nerve supply L_4, L_5, S_1 (superior gluteal nerve).

B, gluteus medius and minimus and tensor fasciae latae muscles as abductors Lying flat on back on firm surface, legs extended, patient attempts against resistance to abduct the leg The muscle can be felt Nerve supply L_4, L_5, S_1 (superior gluteal nerve)

The abnormal mobility distinguishes congenital dislocation of the hips from bilateral coxa vara due to rickety curvature of the femur Poliomyelitis may cause a paralytic limp resembling congenital dislocation but the roentgenologic examination reveals the head of the femur in the acetabulum

Coxa Vara. Coxa vara is a curvature of the neck of the femur, causing adduction of the thigh and apparent shortening of the leg The changes in the position of the neck of the femur in coxa vara may be due in childhood to rickets, in later life to the carrying of heavy burdens or, more rarely, to osteomalacia. The coxa vara of childhood is usually bilateral; that of adults may be either unilateral or bilateral The signs of coxa vara are (1) anterior position and abnormally high position of the trochanter, (2) lateral rotation and limitation of abduction of the thigh, (3) medial rotation and flexion, and (4) when unilateral, shortening and limping

Roentgenograms are diagnostic and should be made unless it is unwise to move an aged, infirm patient

Ankylosis of the Hip Joint. Complete ankylosis of the hip joint is somewhat compensated by a flexible lumbar portion of the spinal column The unfavorable positions of ankylosis of the hip joint are considered to be severe flexion with adduction and internal rotation, since these positions interfere with standing or walking because of the shortening that they produce, which affects lateral equilibrium.

A favorable position of ankylosis is that approaching extension in the long axis of the body. In this position standing and walking are possible but sitting is hampered. Ankylosis in flexion, however, is favorable to the sitting position

Varying degrees of ankylosis of the hip are caused by (1) Contusions or sprains which may result from a severe blow or fall with the impact over the trochanter or imparted through the shaft A single dislocation does not induce more than temporary ankylosis Repeated dislocations may cause stiffening. (2) Fracture of the acetabulum, or of the head or the neck of the femur, may cause stiffness (3) Continuous immobilization over a long period of time may permit of atrophy, adhesions and stiffness. (4) Suppuration in the hip joint usually results in complete ankylosis or a disability just as bad, resulting from joint pain on movement. (5) Rheumatic arthritis in its many forms frequently affects the hip joint

Adduction in a leg that is fully extended at the hip produces disability of standing, balancing, walking, jumping and running The disability in all these activities is increased by the shortening effect, which increases as the adduction deformity increases.

In flexion deformity, abduction is an advantage because it decreases the lengthening effect unless there is external rotation

Internal rotation increases the disability in the performance of all the duties of the leg Outward rotation produces no disability so long as the toes can reach the normal vertical weight-bearing line. When the toes cannot reach the midline, disability becomes more severe, and especially when there is flexion deformity, outward rotation adds to the disability Internal rotation with flexion brings the toes into a more convenient position for weight bearing (McBride)

Tumors of the Hip and Thigh. Of the neoplasms of the hip and thigh those involving the muscle include angioma, fibroma and sarcoma, all of which must be differentiated from tuberculous myositis, gummatous myositis and muscle hernias. Those originating in the bone include cartilaginous exostoses, enchondromas, osteomas and myeloid sarcomas. Such tumors of the bone must be distinguished from osteomyelitis and fractures A spontaneous pathologic fracture of the bone may occur in sarcoma

A positive diagnosis as to the nature of a tumor is established by biopsy

Diagnosis of Hip-Joint Disease. In hip-joint disease there may be no symptoms referable to the hip The pain may be referred to the knee As the disease advances there develops a limp as the result of a shortening of the leg on the affected side. As the leg shortens the pelvis tilts and a scoliosis develops

In a limp from a congenital dislocation of the hip the patient steps forcibly forward on the affected side In these limps the patient obviously is not afraid of producing pain in the leg or foot, but limps in order to place himself more firmly on the affected leg If the dislocation is bilateral, a waddling gait develops A limp may result from painless rigidity of one hip joint, as from a healed coxitis, injury or rickets, the whole extremity, including one half of the pelvis, being moved forward as a unit Bilateral stiffness of the whole lower extremity occurs in extreme bilateral coxa vara, rheumatoid arthritis and from the prolonged use of casts. A limp results when there is pain in some one of the joints on the affected side on movement, as a result all the joints of that side may undergo muscular fixation. The patient avoids

back with the legs straight out, there is obvious lordosis of the lumbar region of the spinal column. If this lordosis is overcome by strong flexion of the thigh of the healthy side, there will be involuntary flexion of the thigh of the affected side when tuberculous coxitis exists (Thomas' test). There is fixation of the affected extremity and the pelvis, these parts moving as a whole

During the progress of the disease a cold abscess may form, pointing in the following order of frequency: (1) in front, below the anterior superior iliac spine, (2) lateralward and (3) backward. Tenderness on pressure can be elicited at the front of the joint below the middle of Poupart's ligament, and compression from the trochanter is painful

Roentgenologic examination in the earliest stages of tuberculous coxitis may not reveal definitely positive findings except for an osteoporosis due to disuse After the disease has advanced and has involved the cartilage and bone, the roentgenologic findings are characteristic and diagnostic

Tuberculous coxitis is distinguished from (1) subacute forms of simple infectious coxitis, (2) chronic infectious arthritis, (3) congenital dislocation of the hip, (4) the different forms of coxa vara, (5) caries of the spinal column and of the pelvis, with cold abscess formation, (6) periappendicular abscess and perinephric abscess, (7) hydrops of the bursa iliaca, (8) sciatica and other neuralgias and (9) hysteria (Brodie's joint).

Nontuberculous chronic coxitis may be either rheumatoid arthritis or osteoarthritis Occasionally the hip is involved in a neuropathic arthropathy such as tabes dorsalis or syringomyelia.

Avascular degeneration of the head of the femur may occur from unknown causes The course is a chronic one characterized by pain which is often referred to the knee. The roentgenologist can usually suggest the correct diagnosis

Injuries of the Hip Joint. If, after an injury to an aged person in the home, roentgenologic examination is not readily available, the following procedures may be helpful diagnostically The position and attitude of the injured extremity should be inspected, for this inspection alone will often give a clue to the nature of the injury. Inspection is followed by measurements, to ascertain whether or not there is shortening, and if so, whether it is supratrochanteric or infratrochanteric

The position of the trochanter is determined by means of the Roser-Nélaton line or by outlining Bryant's triangle The Roser-Nélaton line joins the anterior superior spine of the ilium to the tuberosity of the ischium, normally the greater trochanter of the femur lies in this line. Bryant's triangle is constructed while the patient is lying on the back Let fall a perpendicular line from the anterior superior spine to the table The other side of the triangle is a line joining the anterior superior spine and the tip of the greater trochanter The base of the triangle is a line running horizontally from the tip of the trochanter to the perpendicular line In fracture of the femur the trochanter is elevated, when the neck of the femur is fractured, the base of the triangle is shortened

If it is determined that there is shortening of 1 inch (about 2 5 cm) and there is good reason to believe it was not present before the injury, a dislocation or a fracture has occurred If the shortening is supratrochanteric, there has been a dislocation or a fracture of the neck of the femur, if it is infratrochanteric, there has been a fracture below the tip of the trochanter If the trochanter is abnormally high, it indicates a dislocation or a fracture of the neck If the trochanter occupies its normal position, usually there is no dislocation or, if there is one, it must be situated below the trochanter.

The active movements of the leg are examined by desiring the patient to lie flat on the back and lift the injured leg. If the injured leg can be lifted, there is no dislocation or fracture. If the thigh can be flexed with difficulty, without raising the heel from the bed, an impacted fracture may have occurred, in which event there will be limitation of active medial rotation

thus moved and if such an attempt is made, a sharp pain ensues. A cirsoid femoral vein is soft and yields to pressure and will collapse when the leg is elevated.

THE KNEE JOINT

The knee joint is primarily a hinge joint and is firmly and strongly braced by ligaments. Its movements are extension and flexion. It can be extended to a straight line and flexed until the thigh and the upper portion of the leg come in contact. Any detectable rotary movements of the knee when fully extended are associated with injuries

The bony landmarks of the knee are the patella, the two epicondyles of the femur, the tibia and the fibula.

The patella is pointed distally where the tendo patellae is attached, and is slightly convex on its proximal border. Its lateral edges are prominent, owing to the lack of tissue over this bone With the limb extended and quadriceps muscle relaxed, the patella can be moved in all directions except distally There is a depression above the patella When the muscle contracts, this depression is filled by the rectus, and the muscular swells on each side produced by the vastus internus and externus are visible. When the quadriceps muscle is contracted, the tense tendo patellae becomes evident, when the muscle is relaxed, the soft fatty pad beneath the tendon can be felt.

About halfway between the patella and the tubercle of the tibia can be felt a groove, the line of the joint and the location of the semilunar cartilages. On the lateral side posteriorly, opposite the level of the tibial tubercle, can be felt the head of the fibula Running proximally from the fibula is the tendon of the biceps. In front of the biceps can be seen and felt the iliotibial band of the fascia lata. It is difficult to distinguish the joint line of the knee by palpation.

Posteriorly, with the leg extended, the condyles of the femur can be outlined and recognized The medial is the more prominent The tubercle of the tibia, situated at the insertion of the patellar ligament, can best be seen and felt when the tendo patellae is relaxed. The tubercle of the tibia is not to be confused with the external tuberosity of the tibia, which is proximal and lateral to the tubercle, laterally from the external tuberosity and somewhat distally can be seen and felt the head of the fibula Posteriorly when the knee is extended is seen the fullness of the popliteal space

Extending about 2 inches (about 5 cm) above the patella is the subfemoral or suprapatellar bursa

The capsular structures of the knee in their lower ends are attached to the tibial tubercle, but above, their attachments are far removed from the joint. These structures are so strong and thick that pus from within does not come through but goes around them In maximal extension the bulk of the patella rises above the articular surface, and connecting its upper edge with the anterior surface of the femur is only the thin capsular ligament, hence effusions into the joint bulge upward at this point

Functional Testing of the Muscles About the Knee Joint. *Hamstring Muscles.* The patient in the prone position tries to flex the knee against resistance The tendons of the biceps (laterally) (Fig 6-57A) and semitendinosus (medially) (Fig 6-57B) * can be felt and usually seen (Nerve supply, L_4, L_5, S_1, S_2 Sciatic nerve)

The Knee and Monarticular Disorders. *Infections of the Knee Joint.* The knee joint is affected by both acute and chronic inflammations

In the *acute inflammations* of the knee joint the etiology may be that met with in acute arthritis of any of the joints An acute gonitis is nearly always of infectious nature Gonococcal gonitis is rare, it may localize in one knee joint, and sometimes

* Acknowledgment is made to the Controller of Her Britannic Majesty's Stationery Office for permission to make line drawings of photographs of muscles in action in War Memorandum No. 7, reprinted 1945.

using the affected extremity as a support. The body becomes inclined toward the healthy side.

The diagnosis of disease of the hip joint is made from the history, and the physical and roentgenologic examinations. However, in some instances the exact diagnosis awaits bacteriologic and histologic studies.

THE THIGH

The thigh is composed of the femur and three main sets of muscles, and is supplied and traversed by the femoral vessels and sciatic and anterior crural nerves The femur serves as a support The muscles move the thigh on the trunk, and the leg on the thigh. The thigh muscles are extensors, flexors and adductors

The deep fascia (fascia lata) of the thigh is a strong layer which completely invests the muscles of the thigh and covers the gluteal region Over the saphenous opening the fascial layer is thin and is known as the fascia cribrosa

The *femoral (Scarpa's) triangle* occupies approximately the proximal third of the thigh Its base proximally is formed by Poupart's ligament, its lateral side by the sartorius muscle, and its medial side by the adductor longus Its floor is formed by the iliacus, psoas, pectineus, sometimes a portion of the adductor brevis, and the adductor longus muscles In the depths of this triangle course the femoral artery and vein, the anterior crural nerve, the long saphenous vein and numerous lymphatic vessels. At its proximal and medial part is the saphenous opening, at which femoral hernias make their appearance Psoas abscesses follow the tendon of the psoas muscle down and make their appearance in Scarpa's triangle Also pus from hip-joint disease comes to the surface at the upper part of the triangle on one side or the other of the femoral artery The apex of Scarpa's triangle is a favorite site for ligation of the femoral artery

The lymph nodes of the groin are separated into the superficial and the deep sets The nodes of the superficial set are along Poupart's ligament and along the blood vessels The nodes of the groins drain the lower anterior half of the abdomen, the genitalia, the lower limbs, and the anal, gluteal and lumbar regions

The deep lymph nodes are not constant, and rarely become the seat of infection; but when chronically inflamed, such a node may be mistaken for a femoral hernia. The nodes of the groin communicate with the external and common iliac nodes

Femoral Hernia. Femoral hernia, although often considered to be acquired, is probably the result of a congenital defect The hernia descends through the femoral canal beneath Poupart's ligament to make its appearance at the saphenous opening on the thigh. The saphenous opening has its center 1½ inches (about 4 cm) below and to the outer side of the spine of the pubis The femoral canal represents the narrow space between the femoral vein and the inner wall of the femoral sheath Weakness of the ligamentum lacunare (Gimbernat's ligament), which forms the medial boundary of the femoral ring, is an important factor in the development of a femoral hernia.

Femoral hernia occurs less frequently than inguinal hernia, and more often in women than in men.

The hernia appears in the soft tissues in the femoral region. Such a hernia is smaller than an inguinal hernia and may be present without a mass or other external manifestation or even without the patient being aware of it When strangulation is present, and it occurs often, outward manifestations may be minimal unless the palpating finger presses on the hernia, which is often buried in femoral fat If a loop of bowel is strangulated, however, the manifestations of intestinal obstruction are obvious.

A femoral hernia large enough to contain intestine is obvious. Femoral hernias of this size are not common In an obese patient a strangulation of a small femoral hernia may not be diagnosed until operation for intestinal obstruction is performed.

A small hard femoral hernia has to be differentiated from an *enlarged lymph node, a small lipoma* and *a cirsoid femoral vein* Usually when lymph nodes are enlarged, several nodes are affected. A small lipoma usually can be grasped in the hand and separated from the deep-lying tissue, whereas a femoral hernia cannot be

Stiffness of the knee may be extremely persistent following immobilization of fractures of the leg or thigh Permanent stiffening may occur as a result of atrophy of cartilage, synovial shrinkage and muscular contraction.

Trauma to the knee joint may be followed by loosening of a cartilage from one of the condyles of the femur (roentgenologic examination, palpation); or if there has been a twist of the joint, especially when the thigh has been rotated outward when the leg is fixed, there may be a loosening and displacement of one meniscus, usually the medial meniscus. This causes a disturbance of function of the joint described as internal derangement

Internal Derangements of the Knee. The evidence for internal derangements of the knee is established by the following measures. (1) Eliciting the history ascertains the mechanics by which the lesion was made and the amount and type of pain, swelling, locking or catching, instability, weakness, and limitation of joint motion. Many derangements of the knee which seem of little consequence become disabling owing to the rapid atrophy of the quadriceps muscle, as a result of injuries of the knee. (2) By inspection the degree of atrophy of the quadriceps muscle is seen as well as the range of active and passive motion of the joint, the presence or absence of swelling and fluid, and the location of tenderness if observed Then tests are made for lateral and anteroposterior instability. (3) The roentgenologic examination is usually of value only in a negative way, since the majority of internal derangements affect only the soft tissues, however, it is important in establishing the presence of loose bodies, fractures and calcified meniscuses

Internal derangements of the knee may result from (1) injuries of semilunar cartilages, such as tears, dislocations, cysts, discoid cartilage and calcified meniscuses, (2) loose bodies in the joint such as detached osteophytes, synovial osteochondromatosis, osteochondritis dissecans and osteochondral fractures; (3) injuries of the ligaments; (4) affections of the soft tissues such as cysts and adventitious bursae, hypertrophic infrapatellar fat pads and intra-articular adhesions; (5) fractures of the tibial spine and (6) recurrent dislocations of the patella.

SEMILUNAR CARTILAGES *Tears of the Semilunar Cartilages* These are usually found in young men The history consists of the triad of pain in the knee, swelling of the knee and locking or catching of the knee The triad begins after a twisting injury with the tibia abducted on the femur in case of tears of the medial semilunar cartilage and adducted on the femur in case of tears of the lateral cartilage. The medial semilunar cartilage is injured 10 times more frequently than the lateral semilunar cartilage.

Hypermobile or Dislocating Semilunar Cartilages These probably constitute a definite entity and on occasion can cause locking, but they are rare. Hypermobility may be demonstrated by grasping the anterior end of the cartilage and displacing this toward the midline.

Cysts of the Semilunar Cartilages These are extremely rare, and when present, almost invariably involve the lateral semilunar cartilage. They can often be palpated on the lateral side of the knee.

A Discoid Semilunar Cartilage This represents a congenital defect which usually affects the external semilunar cartilage and is rare. This condition is usually manifest clinically early in life, and the child complains of a snapping sensation in the knee when walking

Calcified Meniscuses These are sometimes seen in older persons and occasionally cause a popping or snapping sensation This condition can usually be demonstrated roentgenologically

LOOSE BODIES. These are the second commonest cause of internal derangement of the knee. The common symptom is locking or catching. In the majority of cases loose bodies can be demonstrated by anteroposterior, lateral or intercondylar notch roentgenograms The bodies may be palpated in the suprapatellar pouch or about the articular surface of the joint. Loose bodies may be the result of:

it causes suppuration there. In polyarthritis due to rheumatic fever the knees are frequently involved

In all acute infections there is evidence of effusion into the knee joint with floating patella, usually there is also some thickening of the capsule, which can be felt in thin persons at its fold of reflection when the affected knee is compared with the healthy knee *Sometimes the cartilages and bones are involved,* as revealed by roentgenograms

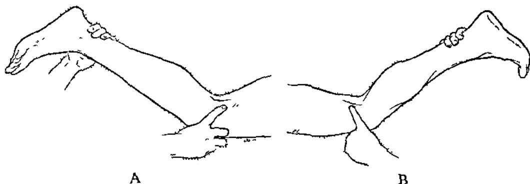


Fig 6-57 Hamstring muscles (semitendinosus and biceps femoris muscles) A, laterally, biceps muscle B, medially, semitendinosus muscle Lying on smooth, firm surface with face downward, patient attempts to flex the knee against resistance The tendon can be felt and seen Nerve supply L_4, L_5, S_1, S_2 (sciatic nerve)

Such acute gonitis must be differentiated from (1) acute prepatellar bursitis, (2) hydrops intermittens of the knee and (3) acute osteomyelitis of the lower end of the femur or of the upper end of the tibia.

Many different forms of chronic inflammation of the knee joint are met with clinically Common causes of chronic effusion into the knee joint are (1) chronic rheumatoid arthritis and (2) tuberculosis.

Effects of Trauma. In falling, the knee often strikes first, and there may be an injury to the bursa prepatellaris, to the patella, or to the knee joint itself

An effusion into the bursa is recognizable from its location and limitations away from the joint When there is an effusion into the knee joint itself, the knee cannot be fully flexed, and there is swelling around the patella, the grooves on both sides of this bone being filled out There may be a transverse swelling above the patella where the joint cavity extends up beneath the tendon of the quadriceps muscle. Effusion into the joint lifts the patella from the condyles of the femur If pressed with the finger down upon the bone, the firm substratum can be felt when it is reached; if the pressure is taken off again, the patella will once more float

In a sprain some of the ligamentous or cartilaginous structures may become permanently damaged The lateral ligaments are the more commonly injured The internal lateral ligament is more commonly injured than the external, and the manifestations may resemble that of injury to the semilunar cartilage The sprain may be severe enough to produce a tear into the bony tissue and in such instances longer and more thorough immobilization will have to be instituted, and thus stiffness of the joint is more likely to occur

Other results *of injury to the knee are those of rupture of the crucial* ligaments, or tearing of the synovial membrane so as to leave a fringe that may be caught in joint action and create chronic synovitis.

True dislocation of the knee *joint is rare and is produced* by extreme violence It is common, however, for the patient to believe that the knee has been dislocated [illegible] or a sprain. True dis- [illegible] *ssociated* with fracture.

tendon Behind the knee joint, in the popliteal space or poples, swelling due to aneurysm is not uncommon; its pulsation quickly differentiates it from (1) distended bursa here, (2) lipoma and (3) cold abscess.

Of the tumors below the knee, sarcoma of the upper end of the tibia or of the fibula is not uncommon. The roentgenogram in such cases is characteristic. Cartilaginous exostoses may also occur near the extremities of both the tibia and the fibula.

THE LEG

The two tuberosities of the tibia, the tibial tubercle and the head of the fibula, can be seen or palpated

The tibia is triangular in shape, with a sharp edge—the crest or shin—forward and a flat surface medially. Thus it participates in the formation of two surfaces, the medial and the anterior, of the leg The medial surface is subcutaneous and extends almost the full length of the leg to the internal malleolus. The lateral surface has the extensor muscles between it and the fibula The fibula, a short distance below its head, becomes covered by the peronei muscles and becomes subcutaneous only in its lower anterior fourth The proximal portion of the leg is largely muscular, but at its distal portion it is mainly tendinous

The muscles of the leg can hardly be considered separately from those of the foot. The long muscles support the arch of the foot, flex, extend, abduct and adduct the foot. Adduction of the foot is associated with a limited amount of rotation.

The individual muscles perform compound action, not a simple one. They act on two joints, the ankle and subastragaloid If the ankle joint is stationary, they abduct and adduct the foot If the subastragaloid joint is stationary, they flex and extend the foot, but if both joints move, as is usually the case, combined action of the muscles accomplishes this feat

The Action of the Muscles as Flexors and Extensors. The movements of the foot when strength is not required are performed by the flexor and extensor groups of muscles. The powerful calf muscles aid especially in lifting and propelling the body forward in locomotion When most of the flexors and extensors of the leg are paralyzed, the foot hangs loose from the leg, the so-called flail foot (drop foot). Weakness of the flexor group (tibialis posterior, flexor digitorum longus and flexor hallucis longus) tends to favor a descent of the arch with consequent pronation or eversion. Weakness of the extensors causes toe drop and inversion or supination.

Paralysis of the calf muscles deprives the posterior pillar of the arch of its support, and the action of the flexors and extensors elevates the arch while the heel descends, so that a condition of hollow foot is produced

The Action of the Muscles as Abductors and Adductors. Lateral movements of the foot are comparatively weak. These movements are for maintenance of equilibrium and adaptation of the position of the foot to uneven surfaces. Three muscles act very distinctly as abductors; they are the peroneus longus, brevis and tertius Two act as distinct adductors, namely, the tibialis anterior and the tibialis posterior

The muscles of the calf act more as abductors than adductors, because the insertion of the Achilles tendon (tendo calcaneus, tendo achillis) is not directly behind the ankle joint but more to its outer side

When the foot is deformed in the position of inversion, as in clubfoot, the tibialis anterior and posterior are usually contracted, but when in the position of eversion, as in flatfoot, spasm of the peronei or calf muscles is frequent.

Plantar flexion of the foot is a far more powerful movement than extension. Flexion is associated with adduction or inversion and extension with abduction or eversion, hence it is that inversion is the position of strength, and eversion of weakness Feats of strength and agility cannot be performed by those who have markedly everted feet.

Detached Osteophytes These occur in persons of later middle age or senility who have had osteo-arthritis for years

Synovial Osteochondromatosis. There are numerous loose bodies from the synovial membrane.

Osteochondritis Dissecans. This condition usually begins between 10 and 19 years of age and probably represents a form of aseptic necrosis of subchondral bone. The loose piece of subchondral bone with its overlying hyaline cartilage may not be present in the joint as a true loose body and yet the patient may have considerable distress in the form of a dull aching pain. The roentgenogram of the intercondylar notch is often invaluable in demonstrating this lesion.

Osteochondral Fracture This type of loose body results from a fracture involving the joint surface whereby a loose fragment is displaced into the joint.

AFFECTIONS OF THE SOFT TISSUES. *Cysts and Adventitious Bursae* These sometimes appear about the ligaments of the knees and may cause pain and disability of the knee

Hypertrophic Infrapatellar Fat Pads These sometimes occur but are probably very rare. This condition may cause a locking or catching sensation as the fat pad is pinched between the articular surfaces of the femur and the tibia.

Intra-Articular Adhesions These sometimes limit the range of motion of the joint or may even cause a catching sensation but rarely a true locking

FRACTURES OF THE TIBIAL SPINE. These really are lesions of the cruciate ligaments A positive diagnosis can be made only by roentgenologic methods and especially by a roentgenogram of the intercondylar notch

RECURRENT DISLOCATION OF THE PATELLA. This lesion is much more often encountered in women than in men and is often on a congenital basis. The patient gives a history of acute episodes characterized by a sudden slipping and locking sensation with severe pain. The knee may remain locked in flexion If the patient is observant, she will state that the kneecap seems to be displaced to the lateral side of the knee and that she usually manipulates it back to its original position, whereupon the acute pain rapidly disappears. The knee after this episode becomes considerably swollen and may be moderately painful for 1 to 2 weeks

Ankylosis of the Knee Joint. The knee joint is of the hinge type but has a slight freedom of action in rotation and lateral mobility so that it is also a gliding joint.

In ankylosis of the knee rigid fixation in extension is more favorable to function, while flexion is less favorable However, slight flexion has an advantage since, by shortening, the foot has more room to pass forward along the ground

Contusion to the knee joint may produce synovitis, followed by adhesions and limitation of motion

Joint swelling of the knee or synovitis with local redness and heat associated with fever is an infectious process, not an injury. Trauma does not produce the symptoms of inflammation as does infection Synovitis of the knee, produced by a strain or sprain, causes swelling and distention of the joint but does not cause fever or a generally reddened, hot, painful joint

In either partial or complete ankylosis of the knee the nearer the motion can approach full extension the less the disability. Fifteen or 20 degrees of flexion, starting from full extension, permits most of the activities of the leg as a support and walking can be carried out with little mechanical interference (McBride).

Tumors and Swellings. Of the tumors in the region of the knee joint, lipoma is the commonest. Occasionally a sarcoma of one of the bones is met with, or a fibroma or sarcoma may originate in the synovial membrane.

Chronic swellings in the neighborhood of the knee joint, other than neoplasm, are commoner. Thus, in front of the joint, swellings are due to (1) *chronic bursitis prepatellaris*, (2) chronic bursitis pretibialis, or (3) bursitis behind the patellar

Peroneus Longus and Brevis. The patient tries to evert the foot against resistance. The tendons can be felt and usually seen (Fig. 6-65). (Sciatic nerve supply, L_5, S_1.)

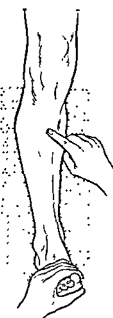




Fig 6-61 Tibialis anterior muscle. Lying on back or sitting, patient attempts to dorsiflex the toes against resistance The tendons can be seen and felt Nerve supply L_4, L_5, S_1 (sciatic nerve).

Fig 6-62. Extensor digitorum longus muscle. Lying on back or sitting, patient attempts to dorsiflex the toes against resistance The muscles can be seen and felt Nerve supply L_5, S_1 (sciatic nerve)

FIG 6-61 FIG 6-62

Small Muscles of Foot. The patient tries to make a cup of the sole of the foot (Fig. 6-66) (Sciatic nerve supply, S_1, S_2) *

Anterior Tibial Syndrome. The anterior tibial syndrome occurs chiefly in young men and consists of ischemic necrosis of the muscles of the anterior tibial





Fig 6-63 Extensor hallucis longus muscle. Lying on back or sitting, patient attempts to dorsiflex the great toe against resistance The tendon can be felt and seen Nerve supply L_5, S_1 (sciatic nerve)

Fig 6-64 Extensor digitorum brevis muscle Lying on the back or sitting, patient attempts to dorsiflex the great toe against resistance The muscle can be seen and felt Nerve supply S_1 (sciatic nerve)

FIG 6-63 FIG 6-64

* Acknowledgment is made to the Controller of Her Britannic Majesty's Stationery Office for permission to make line drawings of photographs of muscles in action in War Memorandum No 7, reprinted 1945

Functional Testing of the Muscles of the Leg and Foot. *Gastrocnemius.* The patient in the prone position tries to plantar-flex the ankle joint against resistance. The muscle belly and tendon can be seen and felt (Fig. 6-58). (Sciatic nerve supply, S_1, S_2.)

Tibialis Posterior. The patient lies on the back and tries to invert the plantar-flexed foot against resistance. The tendon can be seen and felt (Fig. 6-59) (Sciatic nerve supply, L_4, L_5.)

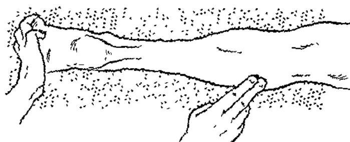


Fig. 6-58 Gastrocnemius muscle. Lying on belly or on side with legs extended, patient attempts against resistance to plantar-flex the ankle The muscle can be seen and felt. Nerve supply S_1, S_2 (sciatic nerve)



Fig 6-59. Tibialis posterior muscle Lying on back with legs extended and abducted, the foot plantar-flexed, patient attempts to invert the foot against resistance The tendon can be seen and felt Nerve supply L_4, L_5 (sciatic nerve).



Fig 6-60 Flexor digitorum, flexor hallucis longus muscles Lying on back, legs abducted and extended and the foot plantar-flexed, patient attempts to flex the terminal joints of the toe against slight resistance. The muscles can be felt Nerve supply S_1, S_2 (sciatic nerve)

Flexor Digitorum Longus, Flexor Hallucis Longus. The patient tries to flex the terminal joints of the toes against slight resistance The muscle bellies can be felt (Fig. 6-60). (Sciatic nerve supply, S_1, S_2.)

Tibialis Anterior The patient tries to dorsiflex the ankle against resistance. The muscle belly and its tendon can be seen and felt (Fig. 6-61). (Sciatic nerve supply, L_4, L_5, S_1.)

Extensor Digitorum Longus. The patient tries to dorsiflex the toes against resistance The tendons passing to the outer four toes can be seen and felt (Fig. 6-62). (Sciatic nerve supply, L_5, S_1.)

Extensor Hallucis Longus. The patient tries to dorsiflex the great toe against resistance. The tendon can be seen and felt (Fig. 6-63). (Sciatic nerve supply, L_5, S_1.)

Extensor Digitorum Brevis. The patient tries to dorsiflex the great toe against resistance. The muscle belly can be felt and often seen (Fig. 6-64). (Sciatic nerve

condition is worse when the patient is resting; then there is an uncontrollable desire to move the legs. Generally speaking, continuous paresthesia points to an organic lesion of the nervous system, while intermittent paresthesia of the type described in this syndrome points to a functional disorder possibly of vasomotor nature.

Massage has no effect, but getting up and walking about may give relief. The disagreeable sensation stops at once on chewing 1/100 grain of nitroglycerin.

Fat Legs and Edema (Lipedema). Those who have lipedema complain of enlargement of the limbs, aching distress in them, particularly during activity, and marked tenderness of the legs. The emotional reaction of patients to this syndrome varies from curiosity relative to its significance to marked evidence of anxiety and tension. In women who are desirous of maintaining a youthful appearance the emotional reactions to the fat legs may be considerable. There are insomnia, nervousness, tenseness, melancholia, anxiety and feelings of frustration. Such a woman is ashamed of her legs or feels that her large legs have ruined her life. These feelings and symptoms are understandable reactions to a disfigurement which is in conflict with the shapely legs of the model for hosiery advertisements. Understandable too is the wearing of long skirts to hide the legs, the avoidance of appearing in swimming suits, and the standing behind chairs at parties

Characteristically, there is symmetric bilateral enlargement of the buttocks and lower extremities which begins almost imperceptibly and progresses gradually. Progressive enlargement of the limbs is ordinarily associated with gain of weight, but evidence of obesity of the trunk, upper extremities, face and neck may be entirely absent, in some instances, there is generalized obesity. The enlargement of the limbs is accentuated by orthostatic activity, particularly in warm weather. Although rest in bed may cause some decrease in size of the legs, it will not cause the limbs to return to a normal size Recurring inflammations, such as are observed in lymphedema, are uniformly absent The feet are normal in size and configuration. There is moderate to great sensitiveness to digital pressure.

THE ANKLE

The ankle is a hinge joint and its motion is anteroposterior except in maximal extension, when a limited degree of lateral movement is possible The range of movement of the ankle is 80 degrees 20 degrees of flexion and 60 degrees of extension

The contour of the ankle is rather uniform, but this uniformity is easily destroyed by diseases and injuries The tibial malleoli form prominences with distinct hollows above and below them The sharp anterior edge of the tibia if followed distally leads to the tibialis anterior tendon On the medial (inner) side the malleolus is large and flat It is subcutaneous and can be readily palpated At its anterior edge is the commencement of the long saphenous vein which runs proximally and slightly back to reach the posterior edge of the tibia About 1½ inch (about 4 cm) distal and in front of the internal malleolus is the prominent tubercle of the scaphoid.

The external malleolus is small and somewhat pointed, and is placed a fingerbreadth distal and behind the level of the internal malleolus Proximal to the tip of the external malleolus is the fibula, which is subcutaneous and readily palpated The transverse line of the joint is level with the upper limit of the swell of the internal malleolus The ankle is covered in front and behind by tendons, most of which, especially in thin persons, can be felt and seen when their muscles are contracted

Posteriorly the tendo calcaneous (tendo achillis) is large and prominent. The posterior tibial artery can be felt pulsating midway between the tendo calcaneus and the internal malleolus The anterior tibial artery can be felt pulsating to the lateral (outer) side of the extensor hallucis longus.

Sprain of the Ankle. In what is usually called a sprain of the ankle the injury is not always confined to the ankle joint and its ligaments In many cases there is a

portion of the leg, with a lesion of the anterior tibial nerve The onset of symptoms is directly related to trauma or physical exertion involving strenuous use of the leg muscles. Unaccustomed exertion causes muscle trauma, which is followed by increased pressure within the anterior tibial region, impaired blood supply to the affected muscles, and ischemic necrosis The anterior tibial nerve is involved either by compression, in which case it recovers rapidly, or by ischemia, in which case the loss of function is permanent The symptoms are pain in the front of the leg fol-

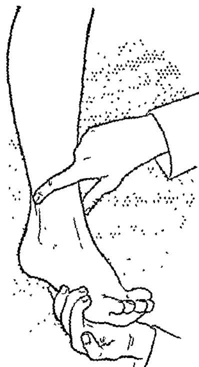


Fig 6-65 Peroneus longus and brevis muscles Lying on back with legs extended and abducted, patient attempts to evert the foot against resistance Tendons can be felt and seen Nerve supply L_5, S_1 (sciatic nerve)



Fig 6-66 Small muscles of sole of foot Lying on back with legs extended, patient attempts to cup the sole of the foot Nerve supply S_1, S_2 (sciatic nerve)

lowed by signs of inflammation over the pretibial muscles and inability to dorsiflex the foot and toes Important negative observations are normal action of the peroneal muscles and a minimal degree of foot drop If the syndrome is recognized early, rest alone may prevent irreversible damage to the muscles

Restless Legs (Anxietas Tibiarum, Leg Jitters). The symptoms are subjective and consist of paresthesias, a feeling of weakness in the legs and a sensation of cold in the feet. The paresthesias occur over the inner aspect of the legs, sometimes in the thighs but rarely in the feet. Characteristically, the crawling sensation develops only when the legs are still, most often after the patient retires for the night Sleep may be disturbed night after night for years with periods of improvement and exacerbation. The disease or syndrome occurs in two main forms. one is characterized mainly by paresthesia and is termed asthenia crurum paresthetica by Ekbom, and the other, in which pain predominates, is termed asthenia crurum dolorosa.

The paresthetic variety is an easily recognizable condition, probably closely related to acroparesthesia and nocturnal burning feet. The painful variety consists of mild to moderate aching localized in the same situations as the paresthesia The

necessitate more work for the long and short muscles and tend to cause foot tire and leg ache.

When all of the weight is borne on the ball of the foot, as in walking on tiptoe, it is called toe-to-toe walking. Toe-to-toe walking imparts greater elasticity and spring to the gait and results in less shock impact than heel-to-toe walking Because of the added elasticity and spring which is secured by toe-to-toe walking, it is used in running, and because it is more graceful, it is used in dancing.

The two tubercles of the calcaneous (os calcis) can be felt posteriorly and at the sides The external surface can be followed forward, but the internal is buried beneath the soft tissues Of the two tubercles on its undersurface the internal can be felt on the sole of the foot by firm pressure

The tubercle of the scaphoid (navicular) lies on the plantar rather than on the lateral aspect of the bone. It can be felt 1½ inches (about 4 cm.) below and in front of the internal malleolus. It is the landmark for the tarsal joints on the inner side of the foot The tibialis posterior muscle runs from it to the posterior edge of the internal malleolus.

The tuberosity of the fifth metatarsal bone is the large bony prominence 2½ inches (about 6 cm) below and in front of the external malleolus. It is the guide to the tarsal joints on the outside of the foot. The tendon of the peroneus brevis runs from it to the posterior edge of the external malleolus

ANKYLOSIS OF THE TOE JOINTS

Complete Ankylosis. Fixed ankylosis of the big toe at the metatarsophalangeal joint is termed hallux rigidus, this is the commonest site of complete ankylosis. This condition may arise as the result of osteoarthritic changes or from severe fracture extending into the joint It may also result from infection and occasionally from operations which involve the joint When ankylosis occurs, a very slight dorsiflexion is of advantage.

The middle phalangeal joint may also become rigidly ankylosed but does not have the importance of the metatarsophalangeal joint The lesser toes may be individually or collectively ankylosed If the metatarsophalangeal joints are fixed in a dorsiflexed position, there occurs a prominence to the ball of the foot so that the anterior arch is obliterated The condition is termed clawfoot

When the middle phalangeal joint becomes ankylosed in a flexed position, the metatarsophalangeal joint is usually dorsiflexed and the condition is termed hammer toe

Partial Ankylosis. Partial limitation of the ankle and tarsal joints is one of the commonest disabilities of the foot Particularly, the plantar flexion deformity is common because so frequently injuries of the leg or foot are treated with the foot in a splint which does not hold it to a right angle

The common causes of partial ankylosis of the toes are (1) contusions or sprains, (2) dislocations, (3) fractures in or near the joints, (4) continuous immobilization, (5) scar contracture, (6) suppuration and (7) rheumatic arthritis

When a toe is examined a considerable length of time after the healing of an injury, the amount of movement that was normal for the toe previous to injury is unknown except by comparison with the movements of the toes of the other foot. On account of the confinement of the toes within the shoe, there is a variation in the shape and motion of toes

ANATOMIC DERANGEMENTS AND FUNCTIONAL DISORDERS OF THE FOOT

Foot Imbalance. Children have one basic type of foot imbalance—*pes planus* The adolescent has two basic types—*pes planus* and *pes cavus*. The adult has both of these imbalances and, as the result, trouble may originate in the anterior arch.

Pes Planus (*Flatfoot*). A flat foot is characterized by inrolling or pronation of the foot and a depression or lowering of the longitudinal arch

tearing off of small fragments of bone; hence the name sprain fracture. Inasmuch as sprains are usually the consequences of lateral displacement, the resultant injury is frequently in the subastragaloid and sometimes in the *adjacent tarsal joints*. A sprain is frequently the result of an inversion, rather than of an eversion, of the foot because in eversion the plantar ligaments are so strong that the foot moves as a whole and the force is transmitted directly to the ankle and leg bones.

A sprain of the ankle is accompanied by pain, swelling and loss of function but there is no subcutaneous ecchymosis

Ankylosis of the Ankle Joint. The ankle joint is a hinge joint with flexion and extension A wide range of motion is provided by the tarsal joints. *The muscle relationship* between the ankle and tarsal joints is correlative.

The common causes of partial ankylosis are contusions, strains, sprains; fractures (*Pott's fracture*), dislocations, continuous immobilization, scar contractures, suppurations and rheumatic arthritis

When the foot cannot be brought to the right angle position, the toe drags as the foot advances Toe drag creates awkwardness and stumbling. Strength, security *and co-ordination are most affected, but quickness and endurance are also decreased* to a degree proportional to the extent of equinus. An individual who must walk on tiptoe has a noticeable deformity and limp

[illegible] the foot cannot

part [illegible]

stab [illegible]

affected so long as the foot can reach a right angle position

When the degree of abduction or pronation is limited to the midline, there is interference in shifting of the weight in taking a step. The gait in the presence of eversion is limited in smoothness and there may be loss of endurance In squatting or jumping there is need of abduction to permit complete dorsiflexion of the foot. Limitation of eversion, however, does not prohibit use of the foot for any particular activity When abduction and eversion are limited to the extent that the foot cannot be brought to the midline, the deformity and limp are obvious.

When the foot is everted and cannot be adducted, there is an increased strain on the arch, and endurance is affected The foot lacks the flexible inward rotation and the weight must therefore be borne mostly on the big toe in taking a step or while standing (McBride)

THE FOOT

The foot provides support for the weight of the body, acts as a lever to raise and to propel it into motion, and when the body is in motion, acts to prevent it from receiving sudden or unexpected jolts.

If standing is too prolonged, ligaments stretch and permit abnormal separation of the foot bones and induce a true foot strain The standing position in which the *foot points straight forward or in which* there is moderate outtoeing is the position in which locking of the bones of the foot is at its maximum and the ligaments are under the least strain.

With the body in motion the muscles play a more important role in supporting the foot than they do with the body at rest, because of the element of postural stability. The long muscles become more important as supports of the arches, since by maintaining the leg in balance over the foot, they prevent abnormal concentration *of weight* stresses on one part of the foot

In heel-to-toe walking, to be efficient, the foot points directly forward in the sagittal plane with each step or at least toes out only 20 to 30 degrees. The foot in the adducted position is, from a structural point of view, in a stronger position than that in which the foot is in the *neutral* or straight position. When the foot toes out more than 30 degrees, the loss of flexibility and interference with smooth action

normal range of dorsiflexion of the first metatarsal bone indicates a hypermobile first metatarsal segment. Callosities under the heads of metatarsals I, II and V and at times over the entire ball of the foot are frequently observed.

In the rigid flat foot the tendons of the peroneus longus and brevis are short and contracted. The lateral mobility of the foot is limited.

The roentgenogram may reveal a short first metatarsal with overdevelopment of the second metatarsal, a metatarsus varus primus with wide separation between metatarsals I and II, a hypermobile first metatarsal segment, or arthritic changes in the foot joints.

DIAGNOSIS. The diagnosis of pes planus is based on the foregoing symptoms and objective findings

Pes Cavus (*High-Arched Foot*). Pes cavus is often congenital but may occur as the result of muscle imbalance secondary to muscle paralysis, especially owing to infantile paralysis, when it is almost invariably due to weakness of the dorsal flexors of the toes and overaction of plantar flexors, plantar intrinsic muscles and heel tendon. Pes cavus also occurs in spastic paralysis due to overaction of muscles

SYMPTOMS. There is pain in the ball of the foot described as a feeling of walking on something hard under the ball of the foot There is tiring in the longitudinal arch of the foot, particularly across the dorsum, and cramping in the calf of the leg Backache is often present if anteroposterior balance is disturbed by a tilting of the pelvis downward and forward

There is less flexibility in the foot as a whole than in a normal or a flat foot.

EXAMINATION With the patient in the standing position, inspection will reveal that the longitudinal arch is abnormally high, the forepart of the foot is somewhat adducted, and the toes are in There may be the appearance of pronation owing to inward rolling of the foot at the ankle joint The line of transmitted weight falls toward the lateral side of the foot, which tends to roll it outward

When the patient sits, it is observed that the Achilles tendon is short, either actually or relatively, because of dropping of the forepart of the foot The ball of the foot is prominent and there is callus formation Tenderness is present over the contracted plantar fascia and over the heads of the metatarsal bones

DIAGNOSIS. The diagnosis of pes cavus is based on the presence of an abnormally high arch, shortening of the plantar fascia, prominence of the ball of the foot, and callus formation There is an absence of pronation, and there is shortening or at least functional shortening of the Achilles tendon Roentgenograms yield very little information

Descent of the Metatarsal Arch and Anterior Metatarsalgia. A depression of the metatarsal arch is associated with either pes planus or pes cavus Disturbances of the metatarsal arch may occur as a separate entity in women more than 30 years of age who have worn improperly fitting shoes

A depressed metatarsal arch is due to improper distribution of weight stresses over the foot as the result of pes planus, pes cavus and improper footwear. High-heeled, pointed, narrow-toed shoes displace the burden of weight-bearing on the metatarsal arch and limit the forepart of the foot and toes in their normal movements.

There is discomfort in the ball of the foot often amounting to acute, cramplike, burning pain in the second and fourth toes. There is loss of the normal dorsal convexity of the metatarsal arch The toes are flexed so that a hammer-toe position is assumed Callus formation often extends across the ball of the foot

Metatarsalgia (*Morton's Toe*) Anterior metatarsalgia represents an advanced form of a depressed metatarsal arch Anterior metatarsalgia is characterized by the sudden onset, while walking, of an acute burning pain in the fourth toe but at times in the second toe This pain is so severe that the shoe must be removed and the toes

ETIOLOGY. Flat feet may result from (1) deformities of the bone, (2) short Achilles tendon (tendo calcaneus, heel cord), (3) muscle inadequacy, (4) ill-fitting shoes and (5) knock knees, bowlegs and tibial torsion.

Deformities of the bones constitute a short metatarsal I, metatarsus varus primus, hypermobility of the first metatarsal segment, and accessory scaphoid, or prehallux, in addition to those resulting from trauma and infection which are so numerous as to be indescribable. The architecture of the foot may be deformed from fracture of bones and loss of the great toe

Hallux valgus develops by depriving the medial side of the foot of the supporting action of the great toe, allowing the foot to pronate, which encourages the descent of the longitudinal arch Fractures of the os calcis commonly cause a depression of the longitudinal arch

A short Achilles tendon prevents dorsiflexion of the foot and shifts the weight-bearing to the anterior part of the foot. The weight on the forepart of the foot causes downward and inward displacement of the subastragalar joint and descent of the longitudinal arch. The pull of a short Achilles tendon tends to displace the os calcis inward and to tilt the subastragalar joint downward and inward, which depresses the longitudinal arch of the foot

Flatfoot may be due to an inability of the muscles to maintain the leg in an approximately vertical plane over the foot. Weakness of the leg and foot muscles may result from illness, obesity or muscle paralysis A commoner cause of muscle weakness is prolonged standing, usually occupational

Shoes having high heels and inadequate length and width may cause foot imbalance. In such shoes the toes are crowded into the forepart of the shoes and thus the weight is borne on tiptoes

Normally the line of transmitted weight of the body passes approximately through the middle of the patella straight downward between metatarsals I and II In the presence of knock knee the line of weight-bearing is shifted through metatarsal I or medial to it With bowleg and tibial torsion the line of weight-bearing falls through metatarsal I or medial to it, just as it does in knock knee, and the weight-bearing thrust is on the medial side of the foot Excessive weight-bearing here rotates the medial side of the foot downward and inward at the subastragalar joint with eventual depression of the longitudinal arch.

SYMPTOMS The first symptom is a tired feeling in the longitudinal arch and the calf of the leg This tired feeling gradually increases in intensity and in time becomes a disabling pain The pain is localized in the region of the scaphoid bone and the subastragalar joint but may include the entire foot Cramping pain in the calf of the leg is often present Pain develops in the knee as the result of the shifting inward of the line of transmitted weight

A downward tilting of the front of the pelvis, accompanied by the secondary upward and forward tilting of the back of the pelvis which may result from extreme instances of inrolling of the feet, increases the work of the lumbar muscles and ligaments and is said to be responsible for the backache in pes planus.

EXAMINATION When making an examination for objective evidence of pes planus or flatfoot, request the patient to stand with the feet parallel and about 3 inches (about 8 cm) apart If there is flatfoot, the longitudinal arch is depressed. The foot is pronated so that the line of transmitted weight falls through metatarsal I or even medial to the inner border of the foot

The scaphoid bone and the internal malleolus are prominent owing to pronation or downward and inward rolling of the subastragalar joint. The great toe is short compared with the other toes. Prominence of the great toe with lateral projection and a broad, splayed-out forefoot are present in metatarsus varus primus.

Tenderness to palpation is usually present in the region of the scaphoid bone and the head of the astragalus and over the plantar surface of the middle cuneiform bone.

The range of dorsal flexion in the male foot with the knee extended and the foot held in mild adduction is 85 or 90 degrees, in the female foot, 90 degrees. An ab-

and the tip of the toe impinges on the ground, it is called mallet toe. This toe deformity gives remarkably little distress in most instances

Congenital hammer toe often involves the second or fifth toe; it is often a familial characteristic but may be observed when the foot is paralyzed.

In rare instances the deformed toe is affected by bursitis In mallet toe a sensitive callosity may form over the end of the toe in close proximity to the nail

Injuries to the Sesamoid Bones. The sesamoid bones of the foot are often irritated, injured, and occasionally fractured. Improper weight-bearing may cause a localized irritation of the sesamoid bones of the great toe joint. Proliferative changes may take place in the sesamoids which increase in size and become irregular in shape; exostoses may even be felt about the margins of such an irritated sesamoid Irritation of a sesamoid is characterized by local pain over the involved bone and tenderness at the same point

Affections of the Tarsal and Metatarsal Bones. ***Köhler's Disease of the Tarsal Scaphoid.*** Kohler's disease occurs in children between the ages of 4 and 7 years and is found more frequently in boys than in girls The cause is a degenerative bone condition which occurs in the young Trauma is a contributing causative factor. Necrotic changes in the cancellous bone with replacement fibrosis have been found.

There is localized pain over the scaphoid bone, aggravated by use and accompanied by a limp Objectively there is tenderness over the scaphoid bone and, at times, swelling Roentgenograms taken in the dorsoplantar and lateral planes show that the tarsal scaphoid is small, dense, often irregular, and narrow in its anteroposterior diameter.

March Foot. March foot is characterized by a painful swelling on the dorsum of the foot, often associated with a spontaneous fracture of one of the metatarsal bones, usually the second or third The condition follows long walks with excessive weight on the back

Interference with the blood supply with weakening of the bones has been suggested as a cause of march foot Extensive use of the forepart of the foot under adverse conditions is the most logical explanation of the condition

When spontaneous fracture occurs, there are periosteal proliferation, fracture of the involved metatarsal bone, and finally, as healing progresses, excess callus formation.

There is pain in the fore part of the foot. Walking is seriously interfered with or is impossible There is swelling over the dorsum of the foot with localized redness and pain There is an area tender to pressure over the distal part of the second or third metatarsal bone If fracture is present, it is impossible to bear weight on the foot After the lapse of a week or two, a roentgenogram will show a periosteal fuzziness at the site of the beginning fracture

Infraction of the Second Metatarsal Bone (*Freiberg's Disease*) This is an affection of the head of the second metatarsal bone occurring in adolescents and characterized by degenerative changes with pain in the metatarsophalangeal joint of the second toe. Trauma plays a contributing role in the causation of the condition

The head of the second metatarsal bone becomes distorted and irregular from degenerative changes There is an accompanying thickening of the shaft of the bone Pain is present over the head of the second metatarsal bone and walking is interfered with There are localized swelling and thickening of the metatarsophalangeal joint of the second toe The joint is tender to pressure and may show evidence of [illegible] plane show char-

[illegible] changes over the tuberosity of the os calcis at the attachment of the plantar fascia may develop into spurs or spurlike prominences Formerly calcaneal spurs were erroneously considered to be caused by a neisserian infection However, systemic infection, local irri-

massaged and manipulated to relieve the discomfort. Attacks of pain tend to become more and more frequent, and the duration more prolonged

The digital nerves come to lie in such a position that they are pressed on. There may or may not be a tumor present which increases the pressure on the nerve. The tumor often present in Morton's toe is either a neurofibroma or an angioneurofibroma The nerve pressed on in metatarsalgia is, as a rule, the fourth plantar nerve which is firmly held down against excursions of the toe by the short flexor of the fourth toe, producing conditions favorable to trauma.

Congenital Clubfoot. Congenital clubfoot occurs about once in each 1,000 births. A hereditary background is ascertained in 5 to 45 per cent of the cases. There are four deformities present in congenital clubfoot: (1) adduction of the forepart of the foot, (2) inversion of the hind part of the foot, (3) equinus and (4) tibial torsion Hart has stated that most children with a congenital clubfoot deformity treated within the first 6 months of life can obtain a functionally normal foot by nonoperative treatment

Hallux. Hallux Valgus (*Bunion*). Hallux valgus is characterized by lateral angulation of the great toe at the metatarsophalangeal joint and enlargement of the medial side of the head of the first metatarsal bone with the formation of a bony prominence which in time becomes covered by a bursal sac.

The basic cause of hallux valgus lies in a weakness of the architecture of the foot There is often a hypermobile first metatarsal segment and there are depressions of the longitudinal and metatarsal arches

Degrees of hallux valgus are commonly present without symptoms. Burning pain at the metatarsophalangeal joint of the great toe is common among those who have symptoms The pain is caused by pressure and irritation of the prominence

There is a lateral deviation of the great toe and the prominence on the medial side of the head of the first metatarsal, as stated, and often a hammer-toe deformity of the second toe is present Depression of the longitudinal arch due to the loss of support of the great toe is often present The metatarsal arch is often depressed and there is callus formation over the head of the second metatarsal bone The bursa over the prominence often becomes distended with fluid and inflamed and even infected, when it may break down with sinus formation

Hallux Varus. Hallux varus is a congenital deformity in which the great toe is smaller than normal and is held projected toward the medial side of the foot, it is usually associated with metatarsus varus.

Tailor's Bunion. A bunion over the tuberosity of the fifth metatarsal bone has been called a tailor's bunion because tailors often have this type of bunion owing to the position in which they sit while sewing. The condition is largely due to friction over the prominent tuberosity of the fifth metatarsal bone by the outer side of the shoe.

Hallux Rigidus (*Hallux Flexus*) Hallux rigidus involves the metatarsophalangeal joint of the great toe There is limitation of motion in this joint It may be associated with hallux valgus Ununited phalangeal fractures cause hallux flexus

"Stumping" trauma to the great toe joint and faulty weight-bearing cause this condition It is often a manifestation of arthritis

Stiffness preventing flexion in the great toe causes foot strain, and pain results on walking. The movements of dorsal and plantar flexion are limited. The toe may become fixed in plantar flexion A ridge of bone is palpable on the dorsum of the great toe joint Roentgenograms taken in the dorsoplantar and lateral planes will show narrowing of the joint space and hypertrophic changes in the head of the first metatarsal bone and the base of the first phalanx.

Hammer Toe. Hammer toe, often developing early in life, is a deformity of one or more toes characterized by acute plantar flexion and rigidity of the midphalangeal joint and extension at the distal phalangeal joint. If the distal joint remains straight

Club Nail (Onychogryposis). Club nail, or onychogryposis, is an excessive hypertrophy of the nail. The nail of the great toe is most frequently affected.

The twisted and thickened nail is generally found in the aged and is thought to be due to an irritation or pressure on the nail end, which in turn irritates the matrix, causing the nail to grow unevenly and at an increased rate. The dorsal layers grow more profusely than do the plantar layers; hence the end of the nail curls downward and the dorsal layers pile up to form a hornlike structure.

The treatment consists in clipping the nail short with heavy bone shears. This will give temporary relief, but the overgrowth of nail generally continues. It is often advisable to soften the nail with salicylic acid or calcium sulfide before clipping. When the club nail is sufficiently enlarged, it should be removed.

DISEASES COMMON TO THE AXIAL AND APPENDICULAR REGIONS AND AFFECTING LOCOMOTION

DISEASES AFFECTING MULTIPLE JOINTS AND LOCOMOTION

The disability in joint disease depends to some extent on the nature of the disease and the kind or class of joint affected Three classes of joints are described, namely, fibrous, cartilaginous and synovial.

Movements About Joints. Bones connected by the various types of joints are capable of the following different kinds of movement

Gliding movement is the simplest kind of motion that can take place in a joint, one surface gliding or moving over another without any angular or rotatory movement.

Angular movement occurs only between the long bones, and by it the angle between the two bones is either increased or diminished It includes flexion, extension, abduction and adduction

Flexion is ventral bending, except at the knee joint, while in the four-footed position.

Extension is straightening out of bones of a joint, hence the reverse of flexion.

Abduction means to draw away from the middle line of the body.

Adduction means brought to, or nearer, the middle line of the body.

Both abduction and adduction have different meanings when used with reference to the fingers and toes In the hand the imaginary line is supposed to be drawn through the middle finger, and in the foot, through the second toe.

Circumduction is that form of motion which takes place between the head of a bone and its articular cavity when the bone is made to circumscribe a conical space by rotation around an imaginary axis, for instance swinging the arms or legs

Rotation is a form of movement in which a bone moves around a central axis, often an imaginary one, without undergoing any displacement from this axis No part of the body is capable of perfect rotation, like a wheel, for the simple reason that such motion would necessarily tear asunder all the vessels, nerves and muscles which unite it with other parts

Joint Pain. Pain is experienced when any of the sensitive structures of the joint are stimulated with a faradic or direct current, or by pinching, tearing, burning with a cautery or acid, cutting with a knife or chisel, or sticking with a needle. Thus the *structures of a joint are all sensitive* to acute injury.

A painful stimulation or injury of fascia, tendons and periosteum, according to McEwin, gives rise to pain felt at the corresponding site of injury distal to it

The stimuli which originate pain in traumatic lesions and in such derangements of a joint as occur in osteoarthritis are likely due to mechanical tearing and squeezing which stimulate the nerve endings and secondarily give rise to inflammatory edema which presses on nerve endings and exerts tension on the nerve networks. In infections of the joints, inflammatory edema and toxic or chemical irritants released as part of the inflammatory process are sufficient in themselves to cause joint pain Less is known about the mechanism of pain production in *periarticular painful conditions* such as the arthralgias and fibrositis

tation caused by faulty foot attitude, and acute or repeated trauma are etiologically important.

There is pain in the heel over the tuberosity of the os calcis aggravated by weight-bearing. There is a definite point of acute tenderness over the tuberosity of the os calcis. A lateral roentgenogram will show proliferative changes over the tuberosity of the os calcis and frequently, but not always, a true spur formation.

Calcaneal Apophysitis (*Epiphysitis of the Os Calcis*). The epiphysis of the os calcis lies at the tip of the heel and receives the attachment of the Achilles tendon It consequently may be partially separated in childhood by excessive strain exerted through the Achilles tendon, and symptoms may develop which resemble apophysitis Apophysitis represents a true degenerative affection involving the epiphysis. It occurs most often in boys between the ages of 10 and 15 years.

The etiology of apophysitis is unknown It may result from (1) direct trauma or strain from the attachment of the powerful heel tendon; (2) circulatory or nutritional disturbances of the epiphysis, probably secondary to trauma or (3) systemic infections

The first symptom is usually a slight limp which is followed by definite pain localizing on the posterior aspect of the os calcis at the tip of the heel. An area of tenderness over the tip of the heel may be elicited by the lateral palpation of the heel with the index finger and thumb Usually the line of tenderness to pressure follows the outline of the calcaneal epiphysis There is, at times, some swelling of the lateral and medial aspects of the heel and, in cases of long standing, edema may be present. A roentgenogram taken in the lateral plane will show the epiphysis to be irregular and segmented with areas of increased density

Tenosynovitis of the Achilles Tendon. This condition is similar to tenosynovitis involving any tendon sheath The condition is characterized by local pain, swelling and redness over the Achilles tendon and crepitation over the tendon on movement.

Bursitis. The bursa most commonly involved is the retrocalcaneal bursa, which lies between the os calcis and the Achilles tendon Inflammation of this bursa is characterized by local pain, tenderness, and swelling The swelling, when present, is localized on the sides of the Achilles tendon Local periostitis with proliferative changes and irregular spur formation on the posterior surface of the os calcis are occasionally found associated with inflammation of this bursa and may be the cause of the bursitis If the bursitis does not subside under conservative measures, the bursa should be excised

Friction of the heel counter of the shoe may cause bursitis of the superficial calcaneal bursa which lies between Achilles tendon and the skin. Such a superficial bursitis can usually be relieved by the application of heat and protecting the area by an adhesive strapping

AFFECTIONS OF THE NAILS

Ingrowing Toenail (Onychocryptosis—Onychia) Onychocryptosis is an acute inflammatory reaction, often frank infection, of the soft tissues at the corner of the nail of a toe. The nail of the great toe is most often involved.

On observation of the stance of the foot in individuals complaining of ingrowing toenails, faulty foot balance will usually be found. Pointed shoes which make pressure on the nail of the great toe, careless and improper trimming of the nails, and excessive width and abnormal convexity of the nail result in local irritation and may eventually cause an ingrowing nail.

Pain, tenderness, swelling and redness at the corner and along the lateral margin of the nail characterize the affection Frequently there is frank infection of the involved area with pus formation, subsequent to which the skin breaks down and a discharging area covered with sluggish granulations develops.

coccus The bacteria may reach the synovial tissue by hematogenous dissemination, invade the joint by direct extension from a suppurative process in adjacent bone, such as osteomyelitis, or they may be introduced into the joint cavity by a penetrating wound.

The synovial tissue is hyperemic, swollen, thickened and infiltrated If suppuration continues for several weeks, the result is ulceration and irreparable destruction of the articular cartilage When there is severe damage of the cartilage, ankylosis results. Abscesses may form in the marrow of the subchondral bone The soft periarticular structures often become acutely inflamed

SYMPTOMS The onset is often sudden with fever, chills, sweats, malaise and anorexia. The joint is tender, red, warm, swollen and painful. Its capsule is distended by effusion, and the adjacent muscles are in spasm Tenosynovitis and bursitis may be present Commonly the hip, knee, elbow or shoulder is affected although no joint is exempt It is rare that more than one or two joints are affected. In some cases the systemic disease may be so severe and the arthritis so mild that the joint infection is not noticed In others the arthritis may be unaccompanied by constitutional signs, and the probable primary focus of infection remains obscure.

EXAMINATION The joint or joints are red, swollen and tender. There is a definite leukocytosis with a rise in the percentage of polymorphonuclear cells. The erythrocyte sedimentation rate is elevated Blood culture will often reveal the causative microorganism before chemotherapy The synovial fluid is cloudy or frankly purulent and the leukocytes may number more than 100,000 per cubic millimeter with more than 90 per cent polymorphonuclear cells. On bacteriologic examination (both smear and culture) of aspirated synovial fluid the organism causing the arthritis can usually be demonstrated

After the tenth day, long after the disease should have been diagnosed, roent-
[illegible] ment has not been effective, roentgeno-
[illegible] stration of the extent of damage to the

DIAGNOSIS Recovery of the organism from synovial fluid by smear or culture proves the diagnosis. Acute monarthritis of abrupt onset, a red, warm, swollen, exquisitely painful and tender joint, associated with fever, leukocytosis and rapid sedimentation rate, is characteristic of suppurative arthritis

The prognosis as to life is generally determined by the nature of the systemic disease If correct therapy, and this depends on the nature of the infection, is started within the first week of infection, the prognosis is better than when treatment is started later

2 ***Meningococcal Arthritis.*** The incidence of articular complication during the course of epidemics of meningococcal meningitis varies from 2 to 20 per cent.

There are two general types of joint symptoms associated with epidemic meningitis The first type appears during the first few days of the disease, when there may be a transient multiple synovitis which resolves spontaneously without progressing
[illegible]

affected, any other synovial joint may, however, be involved

The joint on examination is acutely inflamed and distended with effusion

A diagnosis of meningococcal arthritis can be proved only by recovery of the organism from the joint fluid The general prognosis is not significantly influenced by the arthritis The bacteremia and arthritis usually respond satisfactorily to sulfonamide compounds (orally) or penicillin (intramuscularly).

3 ***Gonococcal Arthritis.*** Gonococcal arthritis results from a spread of the organisms from the primary focus in the urogenital tract through the lymphatics and blood stream to the synovial tissue. Arthritis usually appears within 10 to 30

The rapidity with which swelling of a joint takes place in some instances seems to determine the intensity of the symptoms This is not borne out in all instances by clinical observation, for a knee joint affected by that strange condition known as intermittent hydrops may swell rapidly and the swelling is not accompanied by pain. Those swellings which appear rapidly and are acutely painful are likely to be associated with more intense inflammation than other swellings. It is well, therefore, to know that swelling due to edema of tissue is painless in the absence of an *inflammation of the joint structures*

Referred pain may be felt in the joints from visceral disease, for example, shoulder pain in coronary artery disease, and, conversely, pain suggestive of visceral disease may be referred from skeletal lesions Pain arising in one joint may be felt in another, for instance, the pain referred to the knee in arthritis of the hip.

The tendency of *emotional shocks* and *stresses* to be followed by exacerbations of symptoms may occur in those who have rheumatoid arthritis The etiology of the arthralgias complained of by psychoneurotic patients is obscure.

POLYARTHRITIS

Various classifications of arthritis, comprising an enumeration of the groups of arthropathies, have been published The groups of arthritis which usually are included are as follows (1) infective, (2) traumatic, (3) joint diseases secondary to peripheral vascular disease, (4) joint disease secondary to blood dyscrasias, (5) allergic arthritis, (6) joint diseases of metabolic origin, (7) neuropathy secondary to disturbances of innervation or psychic control, (8) static or mechanical abnormality—loose bodies in the joint, (9) diseases of unknown or uncertain causes and (10) new growths.

Infective Arthritis. This group includes all forms of arthritis in which a bacterial or a viral etiology is demonstrated There are two groups of infective arthritis (1) the primary specific infection of the joint, which is characterized by bacterial invasion of the joint from without, (2) the secondary specific infection of the joint, which occurs from within although the bacteria may not be demonstrated

The primary specific infection is proved by bacteriologic study, and the bacteria are likewise demonstrated in the joint The bacteria have been carried to the joint by the blood stream The microorganisms which may thus cause joint disease are (1) staphylococci, (2) streptococci, (3) pneumococci, (4) meningococci, (5) gonococci, (6) tubercle bacilli, (7) *Brucella melitensis* (malta fever, brucellosis), (8) *Klebsiella granulomatis* (granuloma inguinale) and (9) *Treponema pallidum* (syphilis)

The secondary infective arthritis, in which the bacteria may or may not be demonstrated in the joint but in which arthralgic or arthritic manifestations accompany the primary disease are (1) scarlet fever, (2) samonellosis, (3) coccidioidal arthritis These arthropathies are considered with description of the primary disease elsewhere in this book.

The systemic diseases in which a filtrable virus is the causative agent, and in which arthralgia and joint changes are present, are dengue fever, measles, mumps, chickenpox, smallpox and Reiter's disease The joint diseases caused by the organisms or virus of dengue, measles, mumps, chickenpox and smallpox are mentioned in descriptions of these diseases. Reiter's disease is discussed in the portion of the text on infective arthritis.

The arthritides caused by the staphylococci, streptococci, pneumococci, gonococci and meningococci are often referred to collectively as *acute pyogenic arthritis*. Acute pneumococcal arthritis, though rare, may occur during the course of convalescence from pneumococcal pneumonia.

1. ***Staphylococcal and Streptococcal Arthritis.*** More than one half of the pyogenic arthritides are caused by the staphylococcus and the hemolytic strepto-

expressed from a sinus. It may be demonstrated by smear or recovered by culture or after inoculation of suitable material into guinea pigs.

DIAGNOSIS. The diagnosis is established by demonstration of the tubercle bacilli in the synovial fluid. A positive reaction to the tuberculin test is only suggestive evidence of tuberculous arthritis. A negative reaction is strong evidence against the diagnosis. A presumptive diagnosis can be made by the roentgenologist.

5. ***Brucellosis*** (*Malta Fever*). Brucellosis is not a common disease of the bone and rarely affects the joints Approximately half of the patients who have brucellosis experience arthralgia or myalgia, although only 10 per cent emphasize bone or joint pains as their chief complaint, and in but a fraction of this group are there objective signs of bone involvement. Permanent joint damage is rarely a result of brucellar infection (see Chapter 17)

There are no pathognomonic clinical features of the systemic infection or the joint involvement A positive culture of blood or synovial fluid is conclusive, but the former is obtained in only 1 of 4 cases and the latter even more rarely. An agglutination test, a complement fixation test, a bactericidal test, a skin test and an opsonocytophagic test have been developed but are difficult technically and of limited value because of false negative as well as false positive reactions. No single one of these tests is diagnostic. A positive culture from tissues is diagnostic.

The duration of brucellosis is variable and may be protracted. About 3 to 4 per cent of patients succumb to the infection. The arthritis does not influence the prognosis significantly It is usually mild and rarely results in permanent deformity. The disease is self-limited and subject to spontaneous remissions

6. **Syphilitic Arthritis.** The reported incidence of syphilitic disease of the joints decreases as the precision of diagnosis of joint disease increases

Arthritis occurs in the course of both congenital and acquired syphilis In the acquired type it may be due either to direct spirochetal infection of the joints or to neurogenic changes (Charcot's joints) secondary to tabes. The latter constitutes about half of the cases in the acquired group.

Generalized aching of the "bones" may be present during the height of the early systemic reaction in acquired syphilis

from 8 to 16 years of age a symmetric, painless synovitis is the commonest form of syphilitic arthritis (Clutton's joints) Interstitial keratitis is often associated The knees are most commonly affected There is bilateral effusion without redness and with only slight pain, tenderness or warmth

A monarticular gummatous arthritis may occur in late tertiary syphilis, congenital or acquired A gumma may arise in bone and extend into an adjacent joint, or it may originate in the synovia or other soft articular or periarticular structures. Swelling with little or no pain and without stiffness, local heat or muscle spasm is characteristic Bone destruction with osteolytic areas is frequently revealed by roentgenograms Response to antisyphilitic therapy is the rule

In those who have a Charcot joint as the result of neurosyphilis the reaction to serologic tests of blood and spinal fluid may be negative Diagnosis is based on the neurologic signs of tabes A Charcot joint also results from syringomyelia. Antisyphilitic therapy is ineffective

The diagnosis is proved by positive findings on biopsy of synovial or juxta-articular tissue A presumptive diagnosis is made on the presence of (1) positive serologic reaction, (2) other stigmas of congenital or acquired syphilis, (3) response to penicillin therapy or (4) characteristic changes in the bones seen in roentgenograms.

Reiter's Disease. Reiter's disease, a secondary specific infection, is due to a filtrable virus, a pleuropneumonic organism. This is a rare form of acute arthritis

days after the initial infection. However, it is said that months to years may intervene between the urethritis and the arthritis.

The onset of symptoms is sudden with fever, chills, and joint pains The constitutional symptoms are not severe enough to direct the attention away from the joint. The joint pains are those of an acute migratory polyarthritis, and often it is from a few days to a week before the localization becomes monarticular.

On examination in the period of the migratory joint pains, there are no definite findings except, usually, an active gonorrhea. As soon as there is localization to one joint, tenosynovitis is present Tenosynovitis occurs more frequently than arthritis, *particularly when the wrists or small joints of the hands or feet are affected.* There are leukocytosis and accelerated sedimentation rate.

Cultures of exudate and synovial fluid yield positive results more frequently than do smears Occasionally, however, the smear is positive and the culture is negative.

The reaction to the gonococcus complement fixation test becomes positive within 10 to 30 days after the onset of the urethritis in 9 of each 10 who have the disease Chemotherapy apparently does not affect the specificity of the test if arthritis has supervened. This test alone does not prove the presence or the absence of gonococcal arthritis. There are [illegible] gonococcal arthritis which distinguish [illegible]

The diagnosis of gonococcal a[illegible] the gonococcus by culture or smear of the synovial fluid Helpful diagnostic points are history of exposure and a characteristic clinical course of the disease. A positive reaction to the complement fixation test and recovery or improvement with penicillin or sulfonamide therapy are only presumptive diagnostic evidence.

4. ***Tuberculous Arthritis.*** About 1 of each 25 who have tuberculous infections have skeletal involvement. A tuberculous spondylitis is the most serious of the bone and joint infections (see tuberculous spondylitis, p. 281).

Tuberculosis of the peripheral joints may result either from direct bacillary invasion of the synovial tissue (tuberculous synovitis) or from penetration into the joint by tuberculous tissue from adjacent diseased bone. The formation of granulation tissue separates the articular cartilage Caseation, abscess and sinus formation may result

SYMPTOMS. In the peripheral joints there is an effusion into the joint. There are no signs of acute inflammation. Articular pain and tenderness are absent until late in the course of the disease. In tuberculous arthritis muscular atrophy is relatively early and prominent.

The commonest complication is usually the primary pulmonary infection. Abscess formation in the paravertebral region or in the vertebral bodies when the spinal [illegible] affected, and in the bone or periarticular soft structures when a peripheral [illegible] plegia may occur It seems that tuberculous bone and joint disease is a common cause of secondary amyloidosis

Tuberculous arthritis follows a protracted course of progressive destruction of bone and articular structures lasting several years Recovery of normal joint function is rare. In no other type of arthritis is the mortality rate so high as in tuberculosis of the spinal column.

EXAMINATION. The involved joint is swollen. The doughy feeling and swelling are due chiefly to edema and infiltration of the synovial tissue Redness of the joint is absent in the advanced stages unless the joint is secondarily infected following aspiration of fluid.

The total and differential leukocyte counts are usually normal The erythrocyte sedimentation rate is elevated. On bacteriologic study the tubercle bacillus will be found in the synovial fluid, synovial tissue or the pus aspirated from an abscess or

ness. Limitation of motion is due to the pain of inflamed joint structures and the associated muscle spasm A distention of the joint cavity may produce but little pain.

The diagnosis of acute traumatic synovitis is usually obvious from the history, the symptoms and the examination Aspiration of the joint is not routinely practiced, but in some instances it may be the surest and sometimes the only way of detecting fluid in the synovial cavity, and it serves the added advantage of revealing the kind of fluid present. Microscopic and bacteriologic investigation of the fluid is often useful and important diagnostically.

Diseases of the Joints Due to Circulatory Disturbances. *Diseases Secondary to Peripheral Vascular Disease.* *Aseptic necrosis of bone and joint* may occur secondarily to an infarct or other localized loss of arterial blood supply to bone adjacent to the joint In some instances there is an intra-articular fracture or a dislocation Aseptic necrosis results in pronounced irregularity in the contour of the articular surface with secondary degenerative joint disease.

Aseptic necrosis never eventuates if full restoration of the contours of the intra-articular surfaces occurs; it therefore differs from traumatic aseptic necrosis in that under favorable conditions restoration of normal articular contours may be expected in this disease

Joint disease and osteomyelitis occur secondarily to disturbances of blood flow during the progress of Raynaud's disease, scleroderma, thromboangiitis obliterans (Buerger's disease), ergotism and periarteritis nodosa

Disease Secondary to Blood Dyscrasias. Hemorrhage into a joint or joints of the extremities is a common manifestation of *hemophilia.* The joint becomes swollen, painful and stiff from intra-articular bleeding. The hemorrhage into the joint may be slight, or so great that pain and swelling continue for weeks Once a joint has been affected, it is likely to be affected again and again After repeated small hemorrhages or a large hemorrhage into a joint has occurred, the joint ultimately becomes ankylosed. One or more deformed ankylosed joints are present in practically every hemophiliac who has reached adulthood

Evidence of increased coagulation time of the blood in association with roentgenologic findings of atrophy of bone and periosteal thickening is sufficient for diagnosis. Pseudohemophilia causes the same sort of joint symptoms.

Allergic Arthritis. Experimental work indicates that there are true allergic forms of arthritis such as those observed during serum sickness and possibly sequential to the administration of drugs, particularly sulfonamide compounds and penicillin The opinion is abroad that sensitivity to foods may cause transient or permanent joint changes, but proof is lacking True allergic arthritis, aside from serum sickness, is rare, the diagnosis should be made with caution

Criep differentiated five types of allergic arthropathies. (1) certain instances of chronic arthritis which are thought to be due to bacterial allergy, (2) articular swelling resulting from sensitivity to a foreign serum or to a drug, (3) certain intermittent hydrarthroses, (4) some instances of Henoch's purpura associated with articular swelling and pain and (5) certain instances of acute transient paroxysmal articular involvement of joints characterized by pain, swelling and limitation of motion

The mechanism of production of symptoms is probably the same as that in urticaria or angioneurotic edema, the shock tissue is the synovial membrane of the joint instead of the skin

Hench has repeatedly stated in his publications that he has not been able to diagnose chronic allergic arthritis.

Intermittent Hydrarthrosis. Intermittent hydrarthrosis may be a manifestation of various joint diseases or of early rheumatoid arthritis The condition often affects the knees bilaterally. In some instances intermittent hydrarthrosis may be allergic in origin.

which is said to be limited to men. It causes mild to moderate constitutional reactions In size this organism stands midway between viruses and rickettsiae.

There is a triad of symptoms; namely, (1) acute polyarthritis, (2) urethral discharge and (3) conjunctivitis The onset is acute and the arthritis, the conjunctivitis or the urethral discharge may come first. There may be fever.

On examination one or more joints, usually of the hands, are red, swollen and moderately tender The urethral discharge may be mild or profuse and is negative for gonococci The conjunctivae are congested and often painful Conjunctival smears and cultures are negative for gonococci. The arthritis lasts for weeks or months and tends to recur.

The diagnosis is made by a process of elimination. The disease is self-limited. Rheumatoid arthritis is to be differentiated

Arthritis Due to Infection by Higher Animal Parasites. Generally the joints seem to be immune from invasion by animal parasites. If joints are affected from parasitic infestations, it is secondarily as the result of a sensitization to a toxin elaborated by the parasite, as has been suggested by Rappaport in a discussion of intestinal amebiasis

Traumatic Arthritis. The term traumatic arthritis applies to various injuries in and about the joints Traumatic arthritis may be caused by trauma applied extrinsically or intrinsically to the joint. It may be manifested either acutely or chronically

Acute extrinsic arthritis is often caused by a single *extrinsic* cause; for instance, the joint is struck a single blow which injures the intra-articular surface of the joint. However, acute joint symptoms are manifested if the structures about the joint are so injured as to result in, for example, a traumatic synovitis. In the absence of an *injury acute fibrositis, myositis, bursitis and tendinitis may occur spontaneously* and may be attributed to injury when there has been none

Often as a result of occupational or recreational repeated trauma chronic arthritis arises. It is not always possible to distinguish this type from some forms of degenerative joint disease such as osteoarthritis As in acute traumatic arthritis, it may be difficult to know whether a chronic joint disease is caused from chronic, spontaneously occurring fibrositis, myositis, bursitis and tendinitis or from trauma

Intrinsic injury of a joint usually causes a chronic disability Acute traumatic synovitis, however, may be due to sprains, strains, or fractures into a joint

Chronic traumatic arthritis may be caused by repeated or continuous minor trauma such as occurs as a result of faulty body mechanics, for instance postural scoliosis or flat feet This type is indistinguishable from osteoarthritis. Chronic traumatic arthritis may originate from avascular necrosis or from loose bodies (joint mice)

An accumulation of fluid in the joint cavity (hydrops, hydrarthrosis) is one of the first symptoms in the joint characteristic of synovitis The presence of fluid in the joint is manifested by pain, swelling, obliteration of the normal bony landmarks of the joint, and a sense of fluctuation on palpation The same reaction may occur in a mild degree when normal joints which have been immobilized for some time are first used

In the knee the fluid lifts the patella from its normal contact with the femur, an effect which can often be demonstrated by lightly punching the patella against the femur, producing an audible or palpable tap

In the hip and shoulder, swelling of the joint may be obscured by the overlying muscle However, a comparison in size with the opposite side reveals the degree of swelling present.

In all forms of acute traumatic synovitis the pain is severe. The intensity and distribution of the pain are enhanced by associated lesions of bone, ligament or tendon. The involvement of these additional structures is detectable by local tender-

ciency, leukemia, polycythemia vera and pernicious anemia. The serum uric acid is constantly elevated in chronic gout.

Therapeutic Test. Colchicine, if given promptly and in sufficient doses, will usually relieve the acute manifestations of gouty arthritis. Other forms of arthritis are unaffected by colchicine.

Neuropathic Arthritis. Joints atrophy when their nerve supply is badly deranged or discontinued. A neurotrophic joint disorder may be secondary to tabes dorsalis, syringomyelia, nerve injuries or leprosy. Hysterical and psychogenic disturbances also cause joint dysfunction.

In syringomyelia and in tabes, disturbances of joints are common Spontaneous fracture may occur from increased fragility. In the Morvan type of syringomyelia there may be gradual disintegration of a fingertip similar to that which occurs in leprosy and in Raynaud's disease.

A perforating ulcer of the leg or foot caused by tabes involves, at first, the soft parts; later on it may cause destruction of the underlying bone.

Charcot's Joint. The pathogenesis of Charcot's joint is not understood However, it is thought that this disorder is a rapidly developing degenerative process in joints lacking the protection of pain and position sense and hence used in an awkward and traumatizing manner

The onset may be gradual or sudden, and the course progressive or stationary One large joint of the lower extremities is usually affected by a painless enlargement and hypermobility. Occasionally, but rarely, the process is multi-articular and symmetric.

The flail joint is enlarged and deformed, and can be painlessly hyperflexed, extended and rotated in several directions. Warmth, redness and tenderness are absent

The diagnosis is made clinically on the basis of a neurologic examination in association with history and complaint. On roentgenologic examination there are usually destructive and productive bone changes with pathologic fractures, disintegration and disorganization of the joint.

Psychogenic Arthropathy. There are functional derangements of joints, without structural change, considered to be psychogenic The hysteric joint belongs in this group Recently considerable emphasis has been placed on what some call psychogenic rheumatism Some observers have believed that these psychogenic conditions, when of long standing, may result in true organic changes.

Psychoneurotic individuals in emotional conflict caused by psychic trauma, fear, anxiety, apprehension or sorrow may experience arthralgia, muscle and tendon aches, stiffness, interference with joint motion and other rheumatic symptoms which resemble arthritis or fibrositis

On examination by physical means there is absence of joint changes. Roentgenologic examination and laboratory observations reveal that organic health is good

In some instances, if a psychoneurosis is present, bizarre deformities which do not conform to anatomic changes are helpful diagnostic features It is difficult to differentiate psychogenic rheumatism from fibrositis In psychogenic rheumatism, however, there is a lack of consistent localization of symptoms, a lack of benefit from analgesics, heat and physical therapy, and there is failure to improve in a warm atmosphere and after mild exercise.

The Static Influences on Joints. An extremity is a static unit, and disturbance in one part of this unit will secondarily affect other parts. This static factor is symptomatically important in any joint disease.

In this connection two interesting changes that are met with about the joints may be mentioned, although they are easily recognized, the beginner may be puzzled

Suddenly, without prodromes, the knees feel stiff. The patient observes that the joints are swollen. There may or may not be pain. After varying intervals the swelling disappears, to recur weeks or months later. Several such attacks may occur without leaving any disability.

The general condition is good. Rarely are there other manifestations of the allergic state

There are no definite diagnostic criteria. The knees are swollen or distended with fluid. The diagnosis is made with caution. It seems, however, that intermittent hydrarthrosis may exist as a separate disease entity.

Joint Diseases of Metabolic Origin. *Gout and Gouty Arthritis.* In gout there is a concomitant disturbance of purine metabolism, and the disease is spoken of as being a metabolic arthritis. The definite etiology is not known. The disease is characterized by (1) often a family history of gout, (2) acute attacks of arthritis with freedom from joint symptoms between attacks unless chronic deforming changes have developed, (3) increased concentration of uric acid in serum and other body fluids, (4) deposition of sodium urate crystals in articular, periarticular and subcutaneous tissues and often uric acid stones in the urinary tract and (5) degenerative changes in the vessels of the kidneys, heart and brain as the disease advances.

At least 9 of every 10 patients who have gout are men more than 30 years of age. The disease occurs in all races, nationalities and social levels irrespective of their manner of living. Excessive ingestion of purine foods or alcohol may provoke an attack of gouty arthritis in those possessing a gouty diathesis but does not cause this error in metabolism Likewise surgical operations, dietary indiscretions, emotional stress, administration of crude liver extract, thiamine, dehydrocholic acid (Decholin) and mercurial diuretics may precipitate an acute attack

SYMPTOMS OF ACUTE GOUT. Within a period of a few hours the affected joint or joints become red, warm, swollen, tender to touch and acutely painful when moved. Weight-bearing is often impossible when the affected joint is in a lower extremity; for instance when the metatarsophalangeal joint of the great toe is affected. The metatarsophalangeal joint of the great toe is affected in about half of the patients, but other toes or joints of the feet, ankles, knees, hands, wrists or elbows may be involved. A moderate fever, leukocytosis and an increased sedimentation rate may be present. The arthritis may be monarticular, or migratory and polyarticular. Joint synovitis with effusion and acute bursitis are often associated. Specific treatment during the attack ameliorates the symptoms within a few days, otherwise, severe symptoms may last for several days or even weeks, until the disease is far advanced. After the acute attack the joint is free of symptoms until the next acute attack. Finally the joints are so injured by repeated attacks that chronic joint disease consisting of swelling, pain, partial or complete ankylosis is present

EXAMINATION. In addition to the tender, red, swollen joint, uric acid tophi may be present. They occur most often about the margin of the ears and less often in the olecranon region and around joints of the hands and feet. If a tophus is suspected, its contents should be removed and examined microscopically for needle-like crystals or chemically by means of the murexide test.

In chronic gout the joints may be found to be in various states of dilapidation; these joints are the source of great agony and total disability.

During the earlier stages or years of the disease the joints may appear normal on roentgenologic examination. As attacks recur, osseous tophi are observed as punched-out regions in the bones of the fingers or, more often, in the bones of the feet.

DIAGNOSIS. The diagnosis is based on the characteristics of the disease as enumerated.

The serum uric acid is increased during the acute attacks. Nongouty conditions which may be associated with an increase in serum uric acid include renal insuffi-

Rheumatic Diseases lists the theories of etiology as follows: (1) an infectious disease, (2) a metabolic disease, (3) a disease with an endocrinologic basis, (4) a disease of the peripheral circulatory apparatus, (5) a disease of the nervous system, (6) a psychogenic disease and (7) a disease of hypersensitivity. Data available now strongly suggest that rheumatoid arthritis belongs to those diseases arising from chronic anaphylaxis or hypersensitivity.

Rheumatoid arthritis is a systemic disorder. The disease affects primarily the interfibrillar substance of connective tissue. This substance is a colloidal, jelly-like material existing in the interstices between cells and fibers of mesenchymal origin. This substance is often termed collagen, and the diseases resulting from disturbances in this substance, collagen diseases

Articular lesions consist of a thickening of the synovial lining. As the disease progresses, the articular cartilage is softer, contains larger ulcerations, and connective tissue appears in the subchondral marrow spaces. The cartilage in time may be destroyed and ankylosis may occur. The cortex of the adjoining bones becomes thin and porous

The *subcutaneous nodules* of rheumatoid arthritis are a characteristic pathologic lesion of the disease. Exudation of plasma and blood cellular constituents is a prominent feature of *rheumatic fever nodules*, which contain, in addition, small focal regions resembling Aschoff bodies In the nodules of rheumatoid arthritis proliferation and degeneration predominate, Aschoff-like nodules are rare, and exudation is not a prominent feature. The blood vessels in these nodules are affected by perivascular infiltrations advancing to diffuse inflammation and degeneration of the entire vessel wall Thrombosis may be present

SYMPTOMS The first symptoms often are fatigue, to the point of exhaustion, lassitude, muscular stiffness, loss of weight and general debility. One or more joints slowly become swollen and painful, and function is hampered. The symptoms may commence with repeated mild attacks of polyarthritis accompanied by pain, swelling and redness of the affected joints, slight fever and tachycardia The joints of the hands usually are affected first. When the feet are affected, the foot pain is most severe after inactivity The pain may be somewhat relieved by activity; this is in contrast to the pain of flat feet, which is relieved by rest and made worse by activity

There are some patients in whom rheumatoid arthritis commenced with an acute polyarthritis, high fever and sweats. The polyarthritis advances rapidly and quickly reduces the patients to semi-invalidism or invalidism within a period of weeks

In almost all instances of rheumatoid arthritis the smaller joints of the hands, particularly the proximal interphalangeal joints of the fingers, are likely to be most severely affected

EXAMINATION A rheumatoid joint is swollen and there are pain and limitation of movement Owing to thickening of the periarticular tissues about the joint and the atrophy of the muscles proximal and distal to it, the joint presents a spindle-shaped appearance There is rarely much fluid in one of these joints. The adjacent bursae and tendon sheaths are frequently involved and swollen.

The muscles about a joint are antagonists The stronger of the antagonists, the flexors, exert more force on the joint, therefore the joint is often found in a flexion contracture. Flexion contractures are likely to be particularly apparent in the hands, wrists, knees, elbows and toes, but almost every joint in the body may be involved In cases of advanced disease fibrous and bony ankylosis may occur, accompanied by subluxation or dislocation of the affected joints.

Muscular weakness and atrophy are often prominent findings in rheumatoid arthritis and in some they are the characteristic features of the invalidism. Atrophy in the muscles of the hands is often advanced However, atrophy occurs in all the muscles of the extremities of which the joints are affected It seems that the atrophy of the muscles is an integral part of the disease and is not solely attributable to disuse and muscular malnutrition Atrophy is not limited to the muscles, joints and

by them: (1) lipoma arborescens and (2) ganglion (see Diseases of Tendons, this chapter).

Lipoma Arborescens. In obese women of about middle life it is very common to find below either the medial malleolus or the lateral malleolus a lobulated, flat, tumor-like mass. This is the well-known lipoma arborescens. It is *very common* and may depend on fatty degeneration of a part of the synovial membrane of the joint.

Joint Diseases Associated With Mechanical Abnormalities. Loose Bodies in Joints. Loose bodies in the joints, such as those resulting from osteochondromatosis, osteochondritis dissecans, loose fragments from *intra-articular fracture*, fractured meniscuses or other foreign bodies, often result in sufficient irritation to produce degenerative joint disease.

When cartilage or bone is torn loose in a joint cavity, the fragments become worn slowly so that they can move freely about inside the cavity, sometimes giving rise to recurring attacks of pain, swelling and disability by their mechanical interference with joint movements Loose bodies in a joint produce symptoms only when they oppose the actions of the joint. The common symptom is locking of the joint, which almost always occurs during flexion. The pain is severe, and often time is required to extend the joint fully after locking. The condition is intermittent. Long intervals may supervene between attacks

The diagnosis is made from the history Often the loose bodies may be visualized on roentgenologic examination when they contain bone or calcified areas.

Spondylolisthesis. This lesion consists of a forward displacement of the body of one of the lumbar vertebrae on the one beneath. The most commonly displaced is the fifth vertebra, which slips forward over the sacrum. The etiology is obscure. The condition seems to be associated with increased lordosis of congenital malformation Surgical intervention may be required The diagnosis is made by the roentgenologist.

[illegible] [illegible]

Classification of these forms of arthritis is not possible; *enumeration can be* made. Such enumerations were published in *Differential Diagnosis of Chronic Arthritis*, by Nutrition Research Laboratories, Chicago, in 1942, and in *Primer on the Rheumatic Diseases*, by the American Rheumatism Association, in 1934 and 1942, and in the *Journal of the American Medical Association* in 1949 Reference *has been made to these sources in this text*

Rheumatoid Arthritis. Synonyms of rheumatoid arthritis are atrophic arthritis, proliferative arthritis, chronic rheumatic arthritis, primary progressive polyarthritis, nonspecific infectious polyarthritis

Five types of rheumatoid arthritis have been defined. (1) the adult type, and four variants. (2) the childhood type (Still's Disease), (3) Felty's syndrome, (4) psoriatic arthritis and (5) rheumatoid spondylitis (Marie-Strumpell arthritis) These diseases were formerly described as separate disease entities. Such descriptions seem to have originated from the fact that rheumatoid arthritis varies greatly in its manifestations in different periods of life It still is not clear that rheumatoid spondylitis is rheumatoid arthritis

1. ***Rheumatoid Arthritis of the Adult Type.*** Rheumatoid *arthritis has a* [illegible] than rheuma- [illegible] 's between the [illegible]

The number and the plausibility of certain current theories of etiology of rheu*matoid arthritis prevent* a definite classification of this disease. A further uncertainty about the cause of this disease has been actuated by the fact that symptomatic improvement follows the use of adrenocortical hormones. The *Primer on the*

liver and spleen in the presence of leukopenia. Some of these patients have subcutaneous nodules of rheumatoid arthritis.

4 ***Psoriatic Arthritis*** (*Rheumatoid Arthritis*). About 3 per cent of patients who have psoriasis have rheumatoid arthritis. This may be only an average tendency for these two diseases to coexist. However, there are those who have psoriasis in whom the arthritic changes occur only in the terminal phalanges of fingers, which show overlying psoriatic lesions of skin and nails. Such may be a distinct form of arthritis, but at present the question cannot be definitely answered.

5. ***Rheumatoid Spondylitis*** (*Marie-Strumpell Arthritis*). Synonyms are spondylitis deformans, spondylitis ossificans ligamentosa or rheumatoid arthritis of the spinal column, ankylosing spondylitis, von Bechterew's arthritis, spondylitis ankylopoietica and spondylitis rhizomelica

The view formerly held that rheumatoid spondylitis was a separate disease entity from rheumatoid arthritis was based on the characteristic course of rheumatoid spondylitis, and difference in response to therapeutic trials.

The etiology of the condition is unknown Presumably it is a form of rheumatoid arthritis often originating in the sacro-iliac articulations, accompanied or followed by inflammation of the apophyseal joints or vertebral facets. It is a disease of young adults and commences between the ages of 20 and 25 years It is 10 times more frequent in men than in women

The manifestations of spondylitis have been arbitrarily divided into three phases: (1) the prespondylitic or early stage, which is characterized by shifting pains of a rheumatic nature in the limbs, thorax and peripheral joints, (2) the "sacro-iliitis" phase during which the patient may be able to carry on his daily work because the discomfort is less marked during the day than at night, several hours after retiring and (3) as the disease progresses, the poker back period which is characterized by pain along the entire spinal column, stiffness and eventual rigidity Rigidity of the spine is not painful though the hip and leg joints are more susceptible to fatigue in this condition

Examination reveals a stiff back with decreased or absent expansion of the thorax during inspiration The degree of disability is largely proportional to the deformity of the spinal column. The spinal column may be bent and ankylosed so far forward that it is difficult for the patient to walk because the head and eyes are directed downward toward the anterior thoracic wall. Lateral deformities of the spinal column may be present, a condition which adds to the disability. This type of ankylosis of the spinal column illustrates well the influence of deformities of the axial skeleton on locomotion

Roentgenologic examination during the prespondylitic stage is not necessary for diagnosis The roentgenogram may be recorded as being negative. The diagnosis can be made from the foregoing history and examination During the phase of sacro-iliitis the roentgenologist may observe definite osseous changes which involve the sacro-iliac articulations As the disease progresses, changes detectable on roentgenologic examination gradually become apparent around the apophyseal joints or articulating facets, the joint spaces appearing narrowed or obliterated. Decalcification of the vertebrae and, still later, calcification of the ligaments is reported by the roentgenologist Gradually the entire spinal column roentgenologically may appear to be fitted with a calcified casing partially obliterating the individual bony structures

The condition may be confused most frequently with osteoarthritis

Once the spinal column becomes fixed, the disease has about run its course. The fixation is permanent.

Rheumatic Fever. T[illegible]
and important forms of [illegible]
association with carditis,

bones, for it often affects the skin. The skin over the crippled extremities is smooth, glossy and atrophic The hands and feet may be cold and dry or cold and wet.

Subcutaneous nodules occur in some patients and are often situated over bony prominences, especially in the region of the elbows and over the ulna just distal to the olecranon They vary in size from those just large enough to be palpable to lesions 3 or 4 cm in diameter. They are not painful. They may become ulcerated and infected The rheumatoid nodule may persist for months to years.

The spleen may be found enlarged A generalized lymph-node enlargement of moderate degree is commonly observed. Iritis and uveitis, often intractable, may accompany or precede rheumatoid arthritis

There is often a hypochromic microcytic anemia of the iron deficiency type which responds little if at all to administration of iron. The leukocyte count, the differential count and the platelets are within normal limits The erythrocyte sedimentation rate is almost always rapid, although a few exceptions of active disease with a normal rate may be seen Hench pays close attention to the trend of the sedimentation rate for he believes it indicates the trend of the disease The roentgenologic appearance of joints varies in different stages of rheumatoid arthritis.

DIAGNOSIS. The appearance and distribution of the joint lesions in those less than 40 years of age which have been described are diagnostic The diagnosis is confirmed by the laboratory and roentgenologic findings At times, in those more than 40 years of age, an extensive survey has to be made in order to differentiate rheumatoid arthritis from degenerative joint disease such as osteoarthritis

DIFFERENTIAL DIAGNOSIS. Rheumatoid arthritis is to be differentiated from degenerative joint disease or osteoarthritis Rheumatoid arthritis is a systemic disease and the patients are sick Osteoarthritis, as a manifestation of aging, affects hyaline cartilage, and the patients are otherwise well Muscular weakness and atrophy and cutaneous changes are commonly associated with rheumatoid arthritis, rarely with osteoarthritis or degenerative joint disease Weight-bearing joints are more often involved in degenerative joint disease, whereas in rheumatoid arthritis the involvement is usually symmetric and generalized. The proximal interphalangeal joints are involved in rheumatoid arthritis, the terminal most often in degenerative joint disease (Heberden's nodes), although occasionally the proximal joints are involved also. In degenerative joint disease subcutaneous nodules are not present, and the erythrocyte sedimentation rate is elevated only slightly if at all Elevation of this value is the rule in rheumatoid arthritis (*Primer on the Rheumatic Diseases*, and in *J.A M.A*, 1949)

There is a chronic type of rheumatic polyarthritis very similar to that of rheumatoid arthritis and differentiable only by a period of observation In chronic gout tophi, an increased serum uric acid concentration and roentgenographic changes serve to differentiate the two Psychogenic joint disease may be differentiated, in some instances only after a period of time.

PROGNOSIS. Some patients who have rheumatoid arthritis recover completely. Often, the disease spontaneously becomes arrested or quiescent at some stage in its course, and the patient is able to carry on activities with limited disabilities. Finally, there are those whose disease advances rapidly to complete invalidism of a most miserable sort It is impossible to forecast the turn of events in an individual patient

2 **Juvenile Rheumatoid Arthritis** (*Still's Disease*) The term Still's disease is employed now to designate the disease of rheumatoid arthritis as it occurs in children. Children who have Still's disease have been observed to carry the disease into adulthood.

In Still's disease the joints have the same appearance as in adult rheumatoid arthritis, and there may be subcutaneous nodules

3. **Felty's Syndrome** (*Rheumatoid Arthritis*). The term Felty's syndrome is employed to designate rheumatoid arthritis which is accompanied by an enlarged

faces. Subsequently the irregularities increase and the cartilage is more deeply affected. The cartilaginous surface may show wide erosions and splits, which penetrate to the epiphyseal bone. Macroscopic fragments of cartilage may be separated and dislodged into the articular space. There is active growth at the periphery of the joint membranes where cartilage and synovial intima form a zone of transitional tissue. Marginal proliferations arise at the juncture of periosteum and fibrous synovial capsule, and from subchondral bone, which produce the bony spurs, lipping or osteophytes. These changes represent an advanced phase of osteoarthritis. True ankyloses do not occur, although calcification and osseous bridges are found in some joints and in interspinous ligaments, leading to variable degrees of rigidity of the vertebral column.

SYMPTOMS. The disease commences with mild stiffness and aching pain in or about the affected joint. Constitutional manifestations are lacking.

Despite the steadily progressive anatomic changes which have been demonstrated in most persons more than 60 years of age, the frequency of symptomatic illness from this process is not great even in older patients. Pain from an osteoarthritic joint is often referred to distant parts, for instance, referred pain from vertebral joints may pass around to the abdomen.

EXAMINATION. On examination passive or active motion, especially in the extremes of range, may produce pain Palpation of the joint during motion may elicit crepitus. Tenderness may be present at the articular margins. There may be spasm and tenderness of the associated muscles As the disease progresses, there is gradual, firm or hard, irregular enlargement of the affected joints. In the terminal interphalangeal articulations there may be tenderness and soft swelling. Generally articulations which are subject to greater strain, such as the knee and hip joints and the lower spinal articulations, show the greater disturbance of function. The terminal interphalangeal joints show greater changes in size and function than the proximal interphalangeal joints. The localization of the disease, however, affords no absolute diagnostic criterion There are no laboratory findings indicative of osteoarthritis.

DIAGNOSIS A progressive but often intermittent articular aching, relieved on rest, with minimal physical signs of joint disease in a middle-aged person without evidence of general illness, suggests the diagnosis of osteoarthritis The diagnosis of advanced osteoarthritis or degenerative joint disease is distinctive when it affects the smaller finger joints of the hands with firm or hard, knobby enlargement leading eventually to ugly deformities and limited range of motion

The phenomenon of referred sensations and pain from the thoracic and lumbosacral segments to the trunk and lower extremities in those who have osteoarthritis is common Neuralgias localized to the occipital, frontal, retrobulbar or other regions of the head may have their origin in foci of cervical spondylosis

The course of osteoarthritis is slowly and steadily progressive over years without severe acute attacks of joint redness and swelling unless the joint or joints are traumatized After acute trauma it may be, for a while, difficult to determine whether the patient has osteoarthritis or rheumatoid arthritis except by roentgenologic examination

NONARTICULAR RHEUMATISM

Often the term nonarticular rheumatism is employed to designate a rheumatic disease that does not affect the joints and that is associated with one or another of a large variety of illnesses. Nonarticular rheumatism is poorly defined clinically and pathologically, so that there is lack of agreement about the prevalence of this protean rheumatic ailment and the importance of differentiating it from arthritis.

Among the diseases associated with nonarticular rheumatism should not be included the many febrile illnesses, particularly infectious diseases of specific causation, which in prodromal or early stages are frequently accompanied by rheumatic symptoms which may constitute the patient's chief complaint. As these ailments progress their nature becomes evident so that differentiation from primarily rheu-

a long time those referable to the heart (see Chronic Disease and Allergy, Chapter 18).

Rheumatic fever either in children or in adults is characterized by (1) migratory polyarticular joint involvement, (2) the presence of carditis, subcutaneous nodules, pleuritis, erythema marginatum and chorea, and (3) a quick response to the anti-rheumatic action of salicylates. The joint involvement is acute and is accompanied by a temperature of 101 to 104 F (38.3 to 40 C), leukocytosis and rapid erythrocyte sedimentation.

The diagnosis can be made on the clinical findings.

Palindromic Rheumatism. Palindromic rheumatism is a rare disease characterized (according to Hench) by multiple afebrile attacks of acute arthritis and periarthritis, sometimes also para-arthritis, with pain, swelling, redness and disability generally of only one, but sometimes of more than one, small or large joint of adults of either sex. The attacks appear suddenly, develop rapidly, generally last only a few hours or days, then disappear completely, but recur repeatedly at short or long irregularly spaced intervals. Despite the frequent recurrences and the transitory presence of an acute or subacute inflammatory polymorphonuclear exudate in articular tissues and cavity, there is little or no constitutional reaction or abnormality in laboratory tests; and no significant functional, pathologic, or roentgenographic residues occur even after years of disease and scores of attacks.

The chief points which distinguish palindromic rheumatism from rheumatoid arthritis are the tendency for only one or two joints to be involved in an attack; the frequent isolated short attacks of para-arthritis, the absence of significant constitutional reactions, and the persistently negative roentgenograms. The greatest and most convincing difference is the persistent absence of chronic arthritis even after many attacks extending through years of the disease There appears to be little or no tendency for the disease to become chronic in a given joint.

Osteoarthritis (*Degenerative Joint Disease, Hypertrophic Arthritis*) The following are several varieties of osteoarthritis, each representing different manifestations of the same disease process. (1) Heberden's nodes (affection of terminal phalangeal joints; (2) malum coxae senilis (morbus coxae senilis, affection of hip); (3) osteoarthritic spondylitis (spondylosis, affection of spinal column) Osteoarthritis may be further subdivided according to the extent of the involvement, as follows: (4) generalized—characterized by hypertrophic changes, principally in the terminal phalangeal joints of the fingers, in the knees and vertebrae, although other joints may be affected, the pathologic changes produced in the articular structures by the wear and tear of daily activity, which are apparent in most people after the age of 50 years, are included in this group, (5) localized—one or two joints are affected which have previously been injured by (a) trauma—secondary osteoarthritis following fractures or injuries, (b) infection, (c) structural abnormality (congenital and acquired deformities acting as stresses), (d) poor posture and (e) muscular imbalance.

The causation of osteoarthritis is unknown The primary change is one of degeneration which is correlated with both advancing age and functional stresses such as weight-bearing. Deterioration of cartilage in the weight-bearing areas, for instance of the knee joint, may be demonstrated in some persons as they approach 20 years of age Osteoarthritis occurs with great frequency and in many joints between the ages of 20 and 40 years and is present in most persons past 60 years of age Contributory factors are occupational stresses, obesity, malposture and habit spasm Wear and tear are also increased by functional derangements or mechanical defects within a joint. The clinical manifestations are seen more often in women than in men Heberden's nodes occur more frequently in women, and a sex-linked hereditary predisposition for this classic feature of osteoarthritis seems to be definite.

Early pathologic manifestations are small pits and irregularities of the articular sur-

examination may be diagnostic. Fragments of the tendon are one source of joint mice.

Chondrodystrophia Foetalis. This disease often is erroneously termed osteogenesis imperfecta and achondroplasia. Chondrodystrophia implies a nutritional disorder of the cartilages in fetal life, which seems to be true. Achondroplasia signifies an entire absence of the normal activity of the cartilage in producing osseous tissue, which in fetal rickets is not true

Chondrodystrophia foetalis is a rare disease of the skeleton beginning in fetal life and affecting those bones preformed in cartilage. Heredity is fully established as an etiologic factor. The characteristic features are present at birth; a moderately enlarged head, depression of the root of the nose, trident hands and remarkably short and curved extremities (micromelia).

Nearly all of these dwarfs die between the seventh and ninth months of intra-uterine life Of those living at birth the majority succumb within the first few months The few who survive the first year or two develop without impairment of their general health and apparently have the same life expectancy as do normal persons If the chest is well formed, since the disease is primarily one of deficient bone growth, after the age of maturity a normal life is expected Many have lived to extreme old age. These survivors are termed chondrodystrophic dwarfs Dwarfs of this type often are featured in sideshows of circuses and carnivals

The adult chondrodystrophic dwarf (achondroplast) presents the same general characteristics as are seen in the fetus There is an abnormal development of the skeletal muscles and short bones which gives a strength relatively much greater than that of the normal man The posture is erect except in the lumbar region, where there is marked lordosis due to the forward tilting of the sacrum The face appears small because of the enlarged calvarium. The nose and the nasal region are flattened, and there is a retraction at the root of the nose. The end of the nose is hypertrophied and rounded The extremities, like the nose, are symmetrically and equally involved by a shortening in the proximal or root segment (rhizomelia) The arms are so much shortened that the fingertips barely touch the crest of the ilium. Complete extension of the elbow joint is impossible and motion in the shoulder articulation is limited The hands are diminutive, short, broad and pudgy The fingers are of about equal length, taper, and distal to the second joint they are separated from each other like the spokes of a wheel, hence the name trident hand (*main en trident*). The legs too are short and the femur and tibia are bowed Malposition of the knee joint and relaxation of the joints of the toes are common The sexual organs often are overdeveloped. An enhanced sexual appetite is common to both sexes.

The principal diagnostic features of chondrodystrophia are the fetal origin, macrocephalic and brachycephalic head, depressed root of nose and prognathous jaws, normal trunk, stunted growth of the extremities with resulting decentralization of the midpoint of the body, bone deformities, lordosis, trident hand, general excess of subcutaneous fat with thickened, loose skin, protuberant abdomen, normal mentality and the roentgenologic findings

Ochronosis. Ochronosis is an indefinite disease entity characterized by darkening of the cartilages of the ears, nose, ribs and in later life of the intervertebral disks. It is a rare disease

Three groups of cases are distinguished respectively by the presence of (1) alkaptonuria, (2) staining of cartilages and tissues from the prolonged use of carbolic acid and (3) staining of the cartilages from melanin, which is a derivative of proteins

In the presence of progressive destruction of the cartilage there are the symptoms of a destructive joint disease such as occur in osteoarthritis.

Transmitted light will help to detect the contrast in color, for instance in the

matic diseases is usually not difficult. Varying degrees of nonarticular fibrous tissue abnormalities are usually associated with different forms of arthritis; this secondary fibrositis contributes significantly to the patient's discomfort and disability. It is important, however, to appreciate that there are many forms of nonarticular rheumatism which occur entirely independently—primary nonarticular rheumatic diseases. This group of ailments includes fibrositis, generalized; fibrositis, localized; lumbago, painful stiff neck; bursitis, periarthritis (para-arthritis), tendinitis (tendon-attachment syndrome), tenosynovitis; fasciitis, panniculitis, herniated subcutaneous fat; herniated muscle, shoulder-hand syndrome; and psychogenic rheumatism, for instance, rheumatic manifestations of psychoneurosis.

PRIMARY NEOPLASMS OF THE JOINTS

Benign Tumors. The benign tumors of the joints comprise cysts, xanthomas, hemangiomas, giant cell tumors and synoviomas These benign tumors are usually not diagnosable by clinical means Roentgenologic examination may or may not be conclusive The diagnosis is made from biopsy of the tissue and histologic examination.

Malignant Tumors. Malignant growths of joints occur with only moderate frequency and may arise from any of the articular tissues Joints may also be involved secondarily by neoplastic processes of the adjacent bone or remote parts of the body These metastatic lesions are especially important when they involve the spinal column and must be kept in mind when back pain is extremely severe.

The diagnosis is established by the history, the physical and roentgenologic examinations and histologic study of biopsy tissue of the tumor. Sarcoidosis, though not a malignant tumor, may produce changes and arthralgias resembling those of malignant tumors of the joints

DISEASES OF CARTILAGE, LIGAMENTS, TENDONS, BURSAE AND FASCIA

CARTILAGE

Injury to Cartilage. At the time of the acute manifestations of joint injury it may be impossible to detect evidence of trauma to cartilage However, the cartilage of a joint may be injured without fracture and perhaps without tear of the joint capsule When a fracture extends into a joint, the joint cartilage is always injured. In such an instance the fluid in the joint will be bloody and will be demonstrable by aspiration.

Semilunar Cartilage. Injury to the semilunar cartilage of the knee may consist of a dislocation or actual rupture or tearing of it The internal semilunar cartilage is most commonly injured by a severe twisting and hyperextension of the knee. Depending on the circumstances and the degree of an injury, it may consist of a detach- [illegible] the knee [illegible] ng of the knee with inability to extend the joint is a [illegible] tally considerable fluid accumulates in the joint Replacement of the cartilage often occurs spontaneously or may sometimes be achieved by cautious flexion and rotation of the tibia. If replacement is successful, it is indicated by the ability to extend the leg completely.

The diagnosis may be established by the forementioned signs when they are acute. However, the condition may not be suspected for a long time. If not, and if there are changes in the density of the cartilage, the findings on roentgenologic

Sacro-Iliac and Lumbosacral Sprain. Back pain and often serious disability attend sacro-iliac and lumbosacral sprains. Local muscle spasm, tenderness and pain on movement are the important manifestations. These disabilities may develop [illegible]

workmen who have sustained injuries of the lower part of the trunk, represent an especially difficult diagnosis. Sacro-iliac and lumbosacral sprains are to be distinguished from coccygodynia and various types of synovitis, neuritis, sciatica and bursitis in the region of the back and hip.

TENDONS

Many tendons move in sheaths which are structurally similar to joints and bursae. They are frequently involved with acute and chronic inflammations when the nearby joint is thus affected. In general, however, tendons are not frequent sites of primary serious disease. Acute infections, wounds and tumors of tendons occur.

Prenatal influences as a cause of disease of the tendons may be manifested by a stenosis of tendon sheaths, for instance, a trigger finger or a snapping finger is often of congenital origin.

Infections of Tendons (Tenosynovitis). Tenosynovitis is characterized by a spindle-shaped swelling of the tendon sheaths, which often move with the tendons. On movement there is pain. The skin may be reddened over the inflamed sheath. On palpation of such a spindle-shaped swelling, grating may be felt on movements of the tendon.

In tenosynovitis of the palm of the hand or of the wrist, if accompanied by a purulent exudate, there often is a severe inflammation. A stiff, deformed hand is too often the sequela of the infection.

The diagnosis can rarely be made of bursitis or tenosynovitis as a separate entity since these conditions so frequently accompany joint disease. Occasionally, as the result of trauma, tenosynovitis of the tendons about the wrist can be diagnosed.

Stenosing Tenovaginitis. Stenosing tenovaginitis of the extensor and abductor tendons of the thumb (De Quervain's disease) is a rather common condition. The disorder may produce considerable disability due to pain in the thumb, wrist and forearm. It is commonest in middle-aged women who use the wrist and thumb excessively. Chronic trauma is the most frequent exciting cause. The pain, at first dull, localizing in the region of the radial styloid and extending into the thumb and hand and up into the forearm, is often neuralgic in character and may be worse at night than in the daytime. It is aggravated by motions of the thumb and wrist. In some cases the syndrome is bilateral. There is swelling over the tendon sheath and localized tenderness over the tip of the radial styloid process. A circumscribed thickening of the tendon sheath may be found on palpation, and frequently a cartilaginous thickening is felt over the styloid process situated under the skin, not adherent to underlying bone, and moving with flexion and extension of the thumb. The pathognomonic sign may be noted on grasping and quickly abducting the thumb ulnarward. The pain over the styloid tip is excruciating. Roentgenologic studies do not reveal abnormalities.

Tuberculous Tenosynovitis. Adams and his co-workers analyzed the diagnostic and therapeutic features in a number of instances of tuberculous tenosynovitis. The youngest patient, complaining of symptoms that had lasted a year and a half, was 15 years of age, the oldest patient was 75 years of age and had had symptoms for 3 years when first seen. The influence of use on incidence was shown by the high involvement of the right hand.

Tuberculosis elsewhere in the body and trauma seem to be predisposing causes

cartilage of the ears. The discoloration of the cartilage and the presence of homogentisic acid in the urine are diagnostically helpful. A biopsy of the skin may be of value.

Osteochondromatosis. Osteochondromatosis is a condition in which cartilaginous and osteocartilaginous bodies are formed within and by the synovial membranes of joints and, occasionally, bursae and tendon sheaths.

The formation of these cartilaginous and osteocartilaginous bodies follows the same stages that occur in the embryonic formation of cartilage. As the bodies increase in size, they may be forced to the surface to become pedunculated. When the pedicles break, as they frequently do, the bodies become avascular and the bone in them dies. The cartilage cells near the surface live, nourished by the synovial fluid. The loose bodies are white and round or oval with a smooth or faceted surface. In number they vary from a few to hundreds.

Osteochondromatosis occurs more frequently in males than in females and is usually monarticular The knee joint is involved by far the most frequently, with the elbow second. Other joints, affected relatively rarely, are hip, shoulder, wrist, ankle, temporomandibular, metacarpophalangeal and interphalangeal. Bursae and tendon sheaths are seldom affected

SYMPTOMS. The symptoms are weakness, aching and progressive limitation of motion of the joint. In due time catching or locking of the joint may occur, although it is usually of a transitory nature followed by slight effusion, pain and stiffness. There is rarely spontaneous pain except with an episode of locking. The minority of patients mention feeling movable masses.

EXAMINATION The joint may be normal to examination. Loose or fixed bodies may be felt The joint capsule is thickened somewhat with moderate effusion present. The motion of the joint may be decreased, although usually not markedly.

DIAGNOSIS. In many instances in which large numbers of bodies are present, they are demonstrable by roentgenogram. Rice bodies (corpora oryzoidea), associated with chronic infections such as tuberculosis, are differentiated with ease microscopically and relatively easily on the basis of history and findings. When there are only a few bodies present, the differential diagnosis may become difficult because loose bodies may be produced in osteoarthritis, in osteochondritis dissecans, and occasionally after trauma. When the bodies are not radiopaque, the conditions in the knee joint must be differentiated from a torn meniscus. In the latter condition the symptoms are relatively more severe, particularly early in the course of the condition

LIGAMENTS

Sprain (Rupture of Ligaments). Trauma often ruptures the supporting structures of a joint but does not involve the joint itself Such injuries are designated as sprains Sprains are to be suspected in every severe injury about a joint, especially if there is exquisite tenderness over the ligaments and not over the bone. A severe pain which develops on certain motions only, is suggestive of a sprain if a fracture is not present

Sprain of the Ankle. It has been shown that in many sprains of the ankle there is a tearing off of small fragments of the bone The term sprain fracture is applied to such injuries

Sprains of the ankle are often the consequence of a lateral displacement. The resultant injury is frequently in the subastragalus and sometimes in the adjacent tarsal joints. This condition is suspected when the pain and swelling are located below and in front of the ankle rather than around the ankle. A sprain, however, is most frequently the result of inversion rather than of eversion of the foot. In eversion, because the plantar ligaments are strong the force is transmitted directly to the ankle and leg bones, and thus the ligamentum deltoideum is ruptured. A Pott's fracture often accompanies this sprain.

tendons or muscles which lie over them to glide smoothly against underlying bone or other structures. In superficial locations the bursae protect underlying structures from trauma inflicted over them. Bursae likewise serve to facilitate skeletal movement.

Some bursae occur naturally. Bursae may form, however, in response to special needs when certain movements are repeatedly used. Some bursae, particularly those about the knee, are continuous with the joint cavity, and they are similar to joints in their reaction to injury

Bursae are rarely the sites of acute pyogenic infection except after injury and infection The commonest lesions of bursae follow trauma, which is sometimes direct and acute, but more often is the result of repeated slight injuries, as observed as the cause of prepatellar bursitis.

Of the almost 150 bursae in the body, all those of clinical importance are situated near the major joints

Acute Traumatic Bursitis. An acute traumatic bursitis may follow direct blows, but more often it results from the same type of forceful movement which gives rise to ruptured tendons or ligaments.

There are so many bursae in the body that the symptoms of acute inflammation and injury cannot be described for each of them Indeed such a description is not necessary, for the symptoms are the same except for their situation, depending on the bursa involved

Often acute traumatic bursitis develops rapidly after a relatively slight injury, provided the bursa has been previously injured by repeated insults or irritations The symptoms are local pain and swelling The pain is severe if aggravated by certain motions The swelling is apparent only in the superficial bursae.

There is often point tenderness over the bursa. The disability frequently is severe on account of the pain, limitation of motion and muscle spasm Occasionally infection develops in the bursa and progresses to suppuration

Chronic Bursitis. Chronic bursitis may follow acute bursitis, but frequently it develops insidiously.

The pathologic changes in chronic bursitis are similar to those in the joint since chronic bursitis is often associated with chronic disease of the adjacent joint Fluid is present and villous overgrowth of the bursal lining occurs In addition, however, calcification of the wall of the bursa is frequent and often is revealed in a roentgenogram.

The symptoms are pain, often severe, brought about or aggravated by certain movements which tend to compress or irritate the bursa.

Tenderness is often localized to the region of the bursa. Swelling may develop because of effusion, which is always present and may be demonstrated by aspiration

The diagnosis can be made on the basis of the situation and localization of symptoms if the examiner is aware that a bursa is situated in that particular location When calcification is present, the diagnosis is made on the basis of roentgenologic examination Excision of the bursa is often indicated and is frequently curative, especially when the bursa is calcified.

FASCIA

Dupuytren's Contracture. This is probably an hereditary disorder which does not become manifest until middle age It is a contracture of the palmar fascia, not of the tendons, and the ulnar side of the palm which causes flexion deformity of the

[illegible]

palpated Herniated fat, opportunely situated, may cause a segmental nerve distribution of pain The small herniations of fat may occur along the sides and lower part of the back.

in some instances. Other tendons may be involved, but the tendons of the wrist are by far the most commonly affected.

The patient complains of a gradually developing, painless or slightly tender mass on the volar aspect of the hand There is stiffness with inability to flex or extend the fingers completely, and diminished strength on grasping The temperature may rise to 99 6 or 100 6 F (37 5 or 38 C).

On examination there is a spindle-shaped swelling along the course of the tendon. Finger motion in the later stages of the disease may cause creaking or grating sounds because of degenerated fibrinous deposits within the tendon sheath—so-called rice bodies. Joint stiffness and a fluctuant mass often indicate osseous disease, which may be proved by roentgenologic demonstration of destruction of the carpus. The diagnosis is proved by biopsy and by inoculation of guinea pigs.

Tuberculosis of the tendon sheaths should receive the same systemic treatment accorded to tuberculosis of the lungs or spinal column. Surgical treatment without knowledge of how the lesion is progressing elsewhere in the body involves the likelihood of operating in the presence of advancing or exudative disease.

Traumatic Tenosynovitis. Traumatic tenosynovitis is rarely serious, but it is a common injury of tendons It produces an inflammation of the sheath with outpouring of an excess amount of the lubricating fluid.

On examination there is local tenderness along the course of the sheath, and use of the tendon produces pain On motion of the tendon creaking or crepitation may be audible Later, fibrous tissue may replace the fluid and fibrin, thereby resulting in limitation of motion.

A dislocation of a tendon may occur so that the tendon leaves the groove it normally occupies and finds a new, abnormal site The tendons commonly involved are the long head of the biceps, the peroneal tendons and the posterior tibial tendon. Treatment consists of operative replacement of the tendon and rest for a week or two until movements without pain are possible

Painful Tendons. Tendons may become inflamed, although more often they are painful without evidence of inflammation, accounting for the symptom complex known as tendon attachment pain This may result from trauma or from more than customary use, with or without regional bursitis. This is a common difficulty, known as tennis elbow, at the attachment of the conjoined tendon onto the humeral epicondyle.

Ganglion. Ganglion is a term applied to a smooth rounded mass (0.5 to 1 5 cm. in diameter) which commonly presents itself in the distal portion of the wrist on the dorsal surface and may be made more prominent by flexion of the wrist. It also occurs on the ventral surface of the wrist and in some other joints, particularly the knee It is found in women much more frequently than in men

Ledderhose has shown that the ganglion originates from the fibrous tissue of the joint capsule as a neoplasm The cystic nature of the tumor is explained by the presence of secreting mesothelial cells or by mucoid degeneration of the fibrous tissue. The lumen of the cyst is commonly a closed cavity, but occasionally it communicates with the wrist joint or a tendon sheath

The first symptom is the presence of the tumor. Later there is pain or discomfort which may result in definite disability

The round cystic tumor attached to a tendon is usually sufficient for diagnosis. Breaking the cyst with a well-directed blow such as that obtained from the flat surface of a book is sometimes followed by cure but is not recommended The tumor, if producing disabling symptoms, should be surgically excised.

BURSAE

Bursae are related to joints in that they are potential cavities lined by modified fibrous tissue or mesothelium which secretes a mucoid lubricant and thus enables

improvement of symptoms by the use of heat and massage and by the administration of acetylsalicylic acid are the characteristic symptoms of primary fibrositis. These same characteristics are observed in rheumatoid arthritis

The differential diagnosis of periarticular fibrositis and rheumatoid arthritis is based on evidence of intra-articular disease (such as an increase in synovial fluid), synovial swelling, and roentgenographic signs of the disease. Indirect evidence comprises capsular swelling, redness and tenderness, loss of weight, anemia, rapid sedimentation rate of erythrocytes, muscular atrophy and limitation of the range of movement of the joints. During the beginnings of either disease the diagnosis may have to wait until the manifestations are definite.

A patient who has *psychosomatic rheumatism* has pain or stiffness which is more adequately described as a sensation of fatigue and weakness than as actual discomfort. The patient feels that movement of an arm or leg is impossible, but when he does move it, the act of movement does not increase the discomfort Pains in psychosomatic rheumatism rapidly migrate beyond all bounds of a nerve and muscle group distribution They go up an arm, down through the body and out through a leg and foot.

Fatigue, especially nervous fatigue, accentuates the symptoms of psychosomatic rheumatism or primary fibrositis. Mental stimulation resulting from a party will relieve the pain of psychosomatic rheumatism for hours This is not so in the case of primary fibrositis

Acute or subacute primary fibrositis usually lasts only a few days or a week or two and disappears without any apparent residua Chronic primary fibrositis may persist for years but the patients usually are able to continue their work and customary activities.

DISEASES OF THE BONES

It is not always possible to determine whether a disease of bone originated in the affected bone itself, in the structures of an adjacent joint or as the result of some systemic disease For this reason uncertainties in regard to classification of some bone diseases are inevitable.

The age of the patient may be helpful in the identification of the nature of a bone disease; for instance, acute osteomyelitis is common in children but is rare in adults Separation of the epiphyses occurs only in children As age advances, however, the bones grow more fragile, and an old person may fracture the neck of the femur by such slight trauma as catching a toe in the bedclothes

When the shafts of the long bones are soft and become curved, deformities arise (for example, bowlegs). It may be possible to demonstrate an abnormal softness by producing a passive curvature If the bones are spontaneously bent near the joints, as in genu valgum, the deformity may be less noticeable Deformities of the feet (talipes), of the hands and of the spinal column make up a large part of common deformities of bones

The common deformities in the spinal column are curvatures with a convexity backward (kyphosis), forward (lordosis) or to the side (scoliosis). Distinction is made between the deformities of curvatures and the angular deformity (gibbus), so characteristic of caries of the vertebrae and those resulting from some fractures.

In the long bones of the extremities curvature arising from softening of the whole bone is most often due to rickets or osteomalacia, whereas angular deformities are due to local affections of the bone such as those resulting from pyogenic organisms, tuberculosis, brucellosis, Paget's disease, hemangioma, metastatic malignant lesions and syringomyelia.

Asymmetric shortenings of the extremities may be due to nervous lesions or to [illegible] epiphyseal cartilage during growth Shortening of one leg causes tilt-

Fibrositis. Synonyms for fibrositis are myofibrositis, muscular rheumatism and myositis. The disease occurs in primary and secondary forms. The *primary* form of fibrositis is a nonsuppurative, acute, subacute, or chronic inflammation of fibrous tissue without demonstrable, systemic disease. It may involve fibrous tissue in any part of the body. *Secondary fibrositis* is a nonsuppurative inflammation of fibrous tissue that is a manifestation of a systemic disease or is due to a local injury or strain. It may be a prominent manifestation of such systemic diseases as rheumatoid arthritis, osteoarthritis, rheumatic fever, gout or lupus erythematosus. It also may be due to gonococcic, streptococcic, staphylococcic or meningococcic septicemia or to the toxemia caused by such diseases as typhoid fever, dengue or influenza. Traumatic fibrositis is secondary to an acute injury. It also may develop insidiously as a result of strains of fascia, tendons or joints owing to poor posture, as observed in scoliosis and flat feet.

The cause of fibrositis is unknown. No changes have been demonstrated in synovial fluid or in the intra-articular membranes.

SYMPTOMS. The symptoms in primary fibrositis may be acute or subacute. Often there are muscle pains and mild discomfort. However, there may be recurrent attacks of varying severity which last only a few days or weeks. The attack disappears without residua but will recur. After several attacks, chronic fibrositis may ensue. Seldom does primary fibrositis start insidiously. A characteristic of primary fibrositis is its variability and its tendency to shift to other regions. Only occasionally in an acute attack will there be a slight rise of temperature and minimal local swelling. A prominent manifestation is subjective stiffness of the affected areas with the very first movements as soon as the patient awakens in the morning. After moderate exercise the affected regions feel better. Later in the day, however, the aching and subjective stiffness may return and get worse. The affected regions seem to "jell" with inactivity and improve with moderate exercise. The subjective stiffness and aching are often affected by changes in the weather, exposure to a draft or air conditioning. Acetylsalicylic acid and local application of heat afford relief.

The *localized forms* of fibrositis give symptoms peculiar to the topographic and anatomic situations, as follows:

Periarticular fibrositis most frequently is the result of trauma, rheumatic fever, rheumatoid arthritis, gout, gonorrhea or periarthritis. It causes local regions of tenderness and may produce swelling of the side of the capsule of the joint. If the disease is acute, the periarticular tissues may be acutely inflamed and painful. Any movement of the joint may be so painful that it cannot be tolerated. If the disease is chronic, inactivity causes subjective stiffness but this is relieved by moderate exercise.

Tendinous and fascial fibrositis most frequently is associated with Dupuytren-like contractions, injury of the supraspinatus tendons, gout, gonorrhea or rheumatoid arthritis that affects the tendons, especially the tendo achillis. It causes localized pain and tenderness, especially when the affected tendon or fascia is stretched.

Perineural fibrositis is an accidental involvement of the fibrous tissue in this situation. It always is associated with periarticular or intramuscular fibrositis near the affected nerve and elsewhere. It produces pain along all or part of the affected nerve. It is particularly likely to involve the intercostal, sciatic and brachial nerves.

EXAMINATION. There is no demonstrable synovitis or intra-articular disease, no juxta-articular atrophy of muscles, no loss of weight, and no roentgenographic evidence of arthritis.

On examination of the affected areas there will be found tender nodules, cords or bands in the muscles, fascia, or articular capsule in about one half of these pa- [illegible] s level and the sedi-

[illegible] elieved by moderate [illegible] ges of weather, and activity, aggravation of symptoms by exposure and by changes of weather, and

movements that do not occur normally in the joint In unimpacted fracture of the neck of the femur the lower extremity can be shortened by compression in the long axis or lengthened by traction in this axis. Such abnormal mobility is associated with local pain; absence of such pain points either to an old lesion or, if recent, to analgesia due to tabes or to syringomyelia.

Palpation may be extended and refined by the use of a probe in case a fistula or a sinus exists. On probing, if the bone is bare, the raw bone can be felt as grating; if it is insensitive, the bone is necrotic.

Ossification of Bones. A knowledge of the normal times for the completion of ossification is important in the diagnosis of many bone disorders of younger patients.

Apart from the clavicle and the majority of the skull bones, which are ossified in membrane, the others undergo intracartilaginous ossification. Interference with the ordinarily regular sequence of ossification of the bone may result from hereditary, congenital or acquired causes The resulting diseases are all rare, and certain ones affect membrane bones, while others affect only those bones preformed in cartilage.

Osteogenesis Imperfecta. *Osteogenesis imperfecta, also designated fragilitas* ossium, brittle bones, osteopsathyrosis and Lobstein's disease, is a rare disease of bones manifested by the presence of multiple fractures after slight trauma. Many instances are associated with blue scleras

Bickel has classified all forms of osteogenesis imperfecta somewhat as follows: (A) *Hereditary Type.* (1) Blue sclera and characteristic roentgenologic changes; (2) white sclera and characteristic roentgenologic changes; (3) blue sclera and atypical roentgenologic changes (B) *Nonhereditary Congenital Type.* (1) Blue sclera and typical roentgenologic changes; (2) white sclera and typical roentgenologic changes

It is impossible to distinguish clinically between the hereditary and the nonhereditary congenital types of osteogenesis imperfecta There is a great variation in the severity of the process, from a disease in the newborn which is so severe as to be incompatible with life, to a suspected condition, which proves to be unrelated, in a patient who is osteogenically healthy

These patients are poorly nourished, short in stature, and deformed. The head tends to be triangular in shape with an increase in its transverse diameter The skulls of infants may feel like parchment, the sutures are open Dentition is poor and the teeth often are soft and carious with a translucent appearance

The axial skeleton is most severely and most markedly affected Scoliosis and kyphosis are frequent and severe. Deformity of the thoracic cage varies and the ribs and sternum often are twisted and molded to conform to the deviations of the spinal column

The deformity of the extremities is dependent on the number of fractures and on the success of alinement of the fragments of bones. In some cases the magnitude of the problem of multiple fractures defeats all attempts at treatment.

Excessive mobility of joints attributable to unusual laxness of the capsule and ligaments may be present. These individuals are prone to have frequent sprained joints and tears of joint ligaments.

Multiple fractures caused by trauma as slight as rolling over in bed are a constant feature. The amount of pain suffered at the time is less than normal In Bickel's series there was an average of 9.2 fractures per case of the hereditary type and of 13 1 fractures per case of the nonhereditary congenital type.

In cases of the *nonhereditary* congenital type the fractures occur earlier, are more frequent and are caused by less trauma than in cases of the hereditary type of osteogenesis imperfecta The fractures are subperiosteal, with little displacement of the ends of the bones but with angulation at the site of the fracture. Many incomplete fractures or regions of absorption (Looser's zones) are revealed roentgeno-

ing of the pelvis, scoliosis and limping. A shortening of the radius or a lengthening of the ulna will cause radial flexion of the hand.

When the bones are softened, as in a severe degree of osteoporosis, or when there has been solution of continuity from fracture, the function of a bone as a supporting organ can no longer be fulfilled On attempting to use the bone as support, so much pain is caused that the attempt is given up. When pain is not felt by a child, the child likely is congenitally insensitive to pain. When pain is not felt by an adult, syringomyelia or tabes dorsalis is suspected.

Local enlargements connected with the skeleton are immobile, a point which helps to distinguish them from masses near the bone, though an external mass may become adherent to an underlying bone and thus be rendered immobile, for instance, a carcinoma of the breast may become adherent to a rib.

The form and the consistency of masses attached to bones, or originating in them, can often be felt on palpation. In unimpacted fracture, crepitation may be palpable When tumors or cysts originate within the bone and lead to atrophy of the bony substance over them, this substance may be reduced in thickness to a thin, paper-like layer that crackles on pressure

In subperiosteal hemorrhage, such as that seen after trauma and in infantile scurvy or, sometimes, in cephalhematoma, new bone may form at the periphery. On palpation a raised circular deformity of bone will be perceptible, which as the palpating hand passes toward the center of the mass, suddenly ceases, giving the impression of a defect in the bone.

On palpation over tumors of bone, especially angiomas, pulsation can often be felt. On palpation of the skull, if a pulsation is observed, it may be due either to a bony tumor or to pulsation of the brain felt through a defect in the bone

In fractures of bones palpation by trained fingers will yield clues to the exact nature of the deformity and displacement In diseases of the upper cervical portion of the spinal column palpation through the pharynx gives access to the vertebral bodies. In diseases of the pelvic bones palpation through the rectum or through the vagina may be helpful in diagnosis

When crepitus is perceived near a joint, the examiner determines whether it is in the joint itself, or due to a fracture of bone or to separation of the epiphysis near the joints In crepitation due to a fractured rib the crepitation may be audible during the respiratory movements Fractures are not always accompanied by crepitation, since the ends of the bones may not be in apposition, owing to marked separation or to erosion of the ends of the bones from tumor, or, again, crepitus will be absent if the fracture is impacted.

In testing the bones for tenderness, gradually increasing pressure and tapping with the fingers may be used. By such tests over long bones and on the spinous processes of the vertebrae, disease of bones and of the spinal column is often localized

Tenderness of the bones may be diffuse, as in leukemia, in the state of exhaustion that follows influenza and rubella, and especially in osteomyelitis, or it may be strictly localized, as in fractures or in bone abscesses. Bone tenderness is commonly present in the neurotic patient.

An important method of eliciting bone tenderness is by compression in the long axis, thus: Press upward from the elbow toward the shoulder in testing the humerus; from the heel toward the pelvis in testing the lower extremity; or from the head or shoulders toward the pelvis in testing the spinal column. In case of suspected impacted fractures, manipulation is carefully performed lest an impaction may be undone which might be desirable to keep

Mobility, where normally there is none, is a sign of solution of continuity, and points either to unimpacted fracture or to pseudarthrosis. To discover such abnormal mobility in the neighborhood of joints, the examiner should try to produce

INFECTIONS OF BONES

(*Inflammatory Osteopathies*)

The infections of the bones comprise osteitis, osteomyelitis and periostitis.

Osteitis. Acute osteitis occurs in conjunction with various bone infections. In the acute form osteitis is rarely a separate entity.

Chronic osteitis is commonly diagnosed by the roentgenologist The clinician can rarely find supporting diagnostic evidence that chronic osteitis is a separate entity. The term also is used to denote diverse bone conditions of noninfectious origin

As a result of infections there often occur (1) atrophy of disuse, (2) subsequent deformities as the result of healing, (3) epiphyseal defects, separations and instability (slipping) and (4) exostosis. During the process of a low-grade infection a fracture may occur, as during syphilitic infections of long bones.

Osteomyelitis. Osteomyelitis may be classified according to its manifestations, as (1) acute (primary), (2) secondary and (3) chronic.

Common sites are the shaft of the femur, the clavicle, scapula, a rib, and the tibia. Any bone may be involved, however, including the bones of the skull, the spinal column, the sternum, and the small bones of the extremities. If the infection of the bone is a virulent one, acute abscesses usually form in and around the affected bone Often a considerable mass of bone dies (necrosis of bone), and the sequestrum will keep up chronic suppuration, with sinus formation, unless an operation is performed.

Acute Osteomyelitis. Acute osteomyelitis is common in childhood, but is rare in adult life It is a hematogenous infection of bone often due to the staphylococcus. The infection may arise from some pre-existing lesion such as a furuncle, septicemia or otitis media However, more commonly it arises through some occult or unknown portal of entry. There is frequently a history of injury at the site of the infection, but its etiologic importance may not be established

Pus under the periosteum strips the membrane from the bone, thus forming a subperiosteal abscess which ruptures into the overlying soft tissue and forms a subcutaneous abscess The amount of bone infected by the disease is not immediately apparent In severe osteomyelitis, when the infection involves the whole medullary cavity, the entire shaft may become necrotic In other instances the infection may break through the cortex so soon that very little bone is invalidated Although the infection rarely penetrates the epiphyseal line, it may precipitate a pyogenic arthritis by entering the joint from without after pus has appeared under the periosteum and extended from there into the joint

There are two reparative processes First occur the separation and partial phagocytosis of necrotic bone, which becomes demarcated from the viable cortex and is called a sequestrum Second, osteogenesis occurs from the lifted-up periosteum, although the new bone, involucrum, cannot be revealed roentgenologically for two or three weeks This new bone, which develops in the presence of the sequestrum, eventually generally becomes dense, hard, and rich in calcium, and replaces the necrotic bone On rare occasions the infection does not extend or penetrate, but forms a localized lesion in bone and is called *Brodie's abscess*, which ordinarily develops insidiously and is really a manifestation of chronic osteomyelitis. From the primary bone lesion metastatic foci may develop, and it is not uncommon for several bones to become infected one after the other. This succession may continue for years so that eventually most of the long bones become invaded by the osteomyelitic process Abnormal lengthening of the affected bone occurs in many children after many months and is apparently due to the increased blood supply, the hyperemia at the epiphyseal line augmenting local bone growth Owing to the preferences of the osteomyelitic process for the tibia, femur, humerus, radius, ulna, fibula and metatarsal bones, the irregularities in length do not cause grave locomotor difficulties. Locomotor disturbances are consequences of the active disease.

SYMPTOMS. The general symptoms are those of general septicemia with fever, chill, rapid pulse and prostration. The extreme pain seems to enhance the prostra-

graphically. The frequency of fractures ceases as puberty is approached and fractures may stop after puberty.

From the foregoing discussion it is clear that only in the rare case without a history of multiple fractures from birth on, is osteogenesis imperfecta likely to be confused with osteitis fibrosa generalisata. The bone disturbance may be first recognized at the age of about 15 or 16 years when roentgenograms reveal a generalized lack of bone density. The very thin, but not decalcified bone rules out the bone disease of hyperparathyroidism The lack of bone density may or may not be accompanied by blue scleras. The concentrations of serum calcium and serum phosphorus are within normal limits. The concentration of serum phosphatase may be slightly elevated. There probably will be a family history of fractures, blue scleras, or otosclerosis. Blue scleras and otosclerosis are not constant features of this disease.

Osteochondrosis of the Capitular Epiphysis (Legg-Perthes-Calvé Disease, Osgood-Schlatter Disease; Köhler's Disease). Osteochondrosis of the capitular epiphysis (Legg-Perthes-Calvé disease, coxa plana) is a disease of the upper part of the femur affecting children between 5 and 10 years of age This disease has been thought to have an infectious element in its etiology and thus the designation osteochondritis deformans juvenilis has been used.

Symptoms comprise slight pain and limp that are soon followed by shortening of the leg This disease may symptomatically resemble coxa vara.

Diagnosis is established by roentgenographic examination The roentgenograms reveal progressive flattening of the head of the femur which is characteristic of the disease. A similar lesion has been described in the tibial tubercle (Osgood-Schlatter disease) and in the tarsal scaphoid (Kohler's disease). Treatment consists of immobilization when pain is present.

Lipochondrodystrophy (Gargoylism or Hurler's Syndrome). This is a rare condition ending in death in childhood. Mental deficiency is associated with malformations of the bones There is dwarfish stature with short neck, curved spinal column, short thick limbs, protuberant abdomen and grotesque face. The nature of the facial peculiarities, somewhat resembling those of cretinism, is not clear Optic atrophy may occur. In many cases enlargement of the liver and the spleen gives rise to suspicion of congenital syphilis. The corneas may exhibit opacities in the deeper layer.

Periodic Arthralgia of Hereditary Origin. Periodic arthralgia is characterized by regular recurrences of pain and often swelling of joints of the extremities, but usually of one or both knees. It is a rare disease. The disease has been known to affect five generations of the same family (Reimann).

The disorder has the characteristics of the Schonlein-Henoch syndrome. Both probably are manifestations of the same underlying cause and represent variant forms of a group of periodic diseases The disorder may begin at any time of life, and the intervals may shorten or lengthen It may last a lifetime or may disappear either spontaneously or in rare instances after certain forms of therapy. Rarely do permanent injury to the joints and other effects on the general health occur The episodes usually recur at regular intervals of 7 to 21 days, last several days, usually without fever or other symptoms or signs, and disappear until the next predictable bout. In some patients recurrences come at irregularly short or long intervals. In some instances there is only stiffness, and in others there is an effusion into the joint or joints.

Biopsy reveals edema of the synovial membrane with or without monocytic cell infiltration of the tissue. Effusion of serous fluid, when present, may contain more than 1,000 cells per cubic millimeter; either polymorphonuclear cells or lymphocytes predominate.

Osteomyelitis of the skull is secondary to compound fracture or a sinusitis. Osteomyelitis is always suspected when an abscess or infected wound located near bone fails to heal and forms a chronic draining sinus.

Roentgenologic examination is required in order to make a diagnosis in secondary osteomyelitis. However, the diagnosis is usually evident from the history, the findings, and the situation and appearance of the lesion.

Chronic Osteomyelitis. Chronic osteomyelitis follows an acute primary or secondary osteomyelitis which has resulted in necrosis of bone The severity of chronic osteomyelitis often depends on the extent of bone killed by the virulence of the infection. An extremity which is the site of chronic osteomyelitis shows considerable muscular and bone atrophy and exhibits one or more draining sinuses leading to the bone. The patient is often shrunken from the toxemia, pain and fever. This disease often is caused by *Salmonella typhosa* after an attack of typhoid fever.

Roentgenologic examination will reveal the extent of the lesion and often will clearly demonstrate the site and size of sequestra

Tuberculosis. The distinction between tuberculosis of the bone and of the joint cannot always be made, since the tubercle bacillus often attacks both structures simultaneously, or seemingly so

Tuberculosis of the Cranial Bones. The infection usually gains access to the middle ear through the eustachian tube and is secondary to infection of the throat, cervical lymph nodes or lungs It may spread from more remote foci, however, by way of the blood stream.

In most cases the process is a sluggish one but in others it progresses rapidly, invading the mastoid bone and the labyrinth. External pachymeningitis, with penetration of the dura resulting in meningitis or formation of tuberculoma, is common The sigmoid sinus may be thrombosed In a few cases tuberculous osteomyelitis of the base of the skull in the anterior fossa has been observed This is apparently due to extension of tuberculous processes in the sinuses and nasal bones

Tuberculous otitis is usually secondary to lesions in the upper respiratory passages The onset is gradual in most cases and is not accompanied by pain. There is a thin, watery discharge at first, but this may later become purulent if secondary infection develops There may be multiple perforations of the drum and later the whole drum may be destroyed. In some cases hearing may be only slightly reduced, in many it is completely abolished A characteristic feature is the presence of paralysis of the seventh nerve, which has been estimated to occur in 40 per cent of all cases. Ford observed cases also in which osteitis of the walls of the orbit resulted in palsies of the third nerve

The infection may extend through the dura, causing tuberculous meningitis or solitary tubercle The latter is most likely to be found in the cerebellar hemisphere or the temporal lobe In instances complicated by pyogenic infections, abscess of the brain or purulent meningitis may result

The diagnosis depends on the evidences of tuberculosis elsewhere in the body, the slow course, absence of pain, the multiple perforations of the ear drum, the frequent presence of facial paralysis and, above all, on the demonstration of tubercle bacilli in the secretions and granulations.

Tuberculous Spondylitis. Tuberculosis of the vertebrae (Pott's disease) is the most serious inflammatory disease of the spinal column, especially in children.

The process is believed to begin in the body of the vertebra and extend to the periosteum, the intervertebral disks and ligaments From 1 to 5 adjacent vertebrae may be affected, and in some there are [illegible] weight-bearing, the bodies of the verte[illegible] kyphos The spinal cord or the spinal ne[illegible] vertebral body extending into the epidural space and compressing them. Generalized or localized tuberculous meningitis may be present Compression of the cord may occur as a result of dislocation and deformity of vertebrae or of the dorsal displacement of a sequestrum

tion. During the first day or two of the disease, before the infection has broken through the cortex of the bone, the pain is severe and it is situated over the end of the bone near the joint. In adults the general reaction is likely to be less marked than in children; subacute and chronic forms are more frequently encountered in which the infection develops slowly.

Streptococcal osteomyelitis differs considerably in its manifestations from osteomyelitis produced by the staphylococcus. The former infection much more commonly occurs as a metastatic invasion of the bone from a primary source such as otitis media or mastoiditis or from a furuncle or carbuncle. The manifestations of the streptococcal osteomyelitis are likely to develop more insidiously than those of the staphylococcal infection. The pain is not so severe; swelling and subcutaneous suppuration develop more slowly and less commonly. There is less destruction of bone, and sequestration is therefore less marked. Many such lesions will subside under proper conservative care without gross suppuration. They are particularly prone to occur in infants.

EXAMINATION. Muscle spasm is often present. The joint can be moved somewhat without increasing the pain. Acute tenderness over the involved bone on deep palpation is one of the earliest signs. In eliciting this tenderness the bone is carefully palpated, starting at some distance from the lesion, which is approached gently and gradually The overlying tissues may be swollen and edematous, but the skin itself is not red or tender during the early stage of the disease. If the infection has been present for several days, there may be evidence of a local abscess, that is, swelling, redness, local heat and fluctuation

DIAGNOSIS. The diagnosis is based on the foregoing findings. The local signs and symptoms are meticulously observed Examinations are repeated at short intervals in order to keep informed in regard to the rapidly developing events. The results of roentgenologic examination are disappointing because the earliest roentgenologic evidence of acute osteomyelitis is absorption of bone, which ordinarily is not demonstrable for a week or more after the onset The diseases which may be diagnostically confusing are acute rheumatic fever, acute pyogenic arthritis and acute cellulitis Involucrum formation requires at least 2 weeks. It is discovered on roentgenologic examination when calcium has become deposited under the elevated periosteum Sequestration may not be demonstrable for an even longer period.

When acute osteomyelitis is suspected, a blood culture, which will often reveal the bacterial cause, should be made It is important to remember that in osteomyelitis during adolescence the urine may contain the etiologic agent.

In the differential diagnosis acute osteomyelitis is distinguished from (1) acute arthritis, especially from acute coxitis, (2) subcutaneous abscess and intramuscular abscess, (3) acute rheumatic fever, (4) ordinary septicemia and pyemia and (5) malarial fever

In general, operation is urgent in staphylococcal infections, not urgent and frequently unnecessary in streptococcal infections.

Secondary Osteomyelitis. This is a bone infection occurring as the result of infection in tissues adjacent to the bone, for instance such as that due to compound fractures.

Secondary osteomyelitis of the jaw often develops by extension from cellulitis about a tooth If the tooth is pulled at the improper time, for instance while the infection is too acute, osteomyelitis is particularly prone to develop and may lead to septicemia

The terminal phalanx may become the site of osteomyelitis during the course of a felon. The other phalanges may be infected secondarily from acute suppurative tenosynovitis. Osteomyelitis of the tarsus is sometimes secondary to penetrating infections and may eventually involve the entire foot. The patella and olecranon are sometimes involved by direct extension from an overlying lesion.

Granuloma Inguinale. Granuloma inguinale of bones occurs during the course of the active infection. The skeletal infection is characterized roentgenologically by osteolytic areas in the bones. In none of the cases so far reported are the roentgenologic changes specific for this disease. Diagnosis is best established by biopsy with search for macrophages containing Donovan bodies (*Klebsiella granulomatis*) when the bone changes occur during the course of granuloma inguinale (see Diseases of the External Female Genitalia, Chapter 7).

Syphilis. Syphilis of the bone may be manifested as chronic periostitis. Syphilitic

either in the secondary or in the tertiary stage of the disease.

During the secondary stage of syphilis a patient who has syphilis of the bone may complain of rheumatic or of neuralgic pains, or of circumscribed tenderness on the bones. The superficial bones (skull, anterior surface of tibia, ulna, metacarpi) are most often painful. The pains are milder in the daytime than at night, when they may become almost unbearable. Nodes, due to subperiosteal deposits, often become palpable.

The usual affection of the bones by syphilis is periosteal gumma formation with necrosis of the underlying bone, followed by ulceration and exposure through the skin or by an extensive osteophyte formation Less common is gummatous osteitis or osteomyelitis with necrosis and erosion of bone

Syphilitic inflammation of the bone may produce a new growth of spongy bone on the surface of the cortex Such proliferations of bone may form a convex layer on the bone cortex which as time passes becomes very hard and solid. However, these cortical layers of proliferated bone are not limited to syphilitic infections, for other nonspecific forms of periostitis can produce the same thing. All of these proliferating bone disturbances occur more commonly in the skull and long bones, especially the tibia, than in other bones

Gummatous osteitis and osteomyelitis may arise in the interior of the bone In the cranial bones the periosteum can be separated by such a process, leaving a coarsely corroded surface If the process is extensive, the skull may be penetrated and destroyed, and left with a ragged hole in it. Comparable gummatous nodes may occur in the tibia, extending into the cortex and marrow cavity, which may circumscribe the bone and cause necrosis of it Gummatous lesions may occur within the marrow cavity and involve it locally or may extend to involve the whole of it without outward evidence of their presence In other instances marrow involvement will be accompanied by a spindle-shaped enlargement of the shaft of the bone

In syphilitic dactylitis there is osteoperiostitis with enlargement and rarefaction and internal destruction of the bone The finger swells and may be easily fractured and subsequent fistula formation ensues When a phalanx or a metacarpal bone is affected, the appearance may resemble that of tuberculosis

In roentgenograms the signs of syphilis of the bone are usually characteristic. Sometimes a circular involvement of the bone is recognizable A positive serologic reaction may not be helpful diagnostically, a negative serologic reaction is definite in that the diagnosis of syphilis of the bone should not be made if the reaction is negative

Syphilis of the bones may resemble tuberculosis, sarcoma, sporotrichosis or even chronic staphylococcic osteomyelitis

Yaws. Yaws is caused by *Treponema pertenue*. In the

man

sheaths are involved which give joint symptoms, but the joint surface is not affected, so that primary joint symptoms are not present.

The serologic reactions are positive. The roentgenologic findings are very much

The spinal nerve roots may be involved by infiltration or by compression when there is collapse of the vertebrae and shortening of the spinal column.

SYMPTOMS The *onset is insidious and* is characterized by pains in the distribution of the spinal nerve roots arising in the affected region of the spinal column In children sleep is broken by night cries as the result of relaxation of the muscle spasm of the vertebral muscles

The pain is usually referred around to the anterior surface of the body. Among other symptoms characteristic of the early stages of the disease are abnormalities of [illegible]

weight, fatigue and perhaps afternoon rise of temperature.

EXAMINATION When the cervical vertebrae are involved, the pain is referred to the occiput, neck, arms or shoulders, depending on situation of the lesion The head may be held rigid, flexed, extended, tilted or rotated to one side. There is strong muscle spasm, and rotation of the neck is resisted. If abscess forms, it may drain into the retropharyngeal space or, less commonly, laterally into the muscles of the neck.

Lesions of the thoracic vertebrae cause the body to be inclined forward. The lumbar lordosis is diminished. The patient walks with caution, often on the toes to avoid jars. When the upper thoracic vertebrae are affected, the shoulders are often elevated and squared. If abscess forms, it drains into the posterior mediastinum and causes dyspnea and cyanosis.

Lesions in the lumbar vertebrae cause increased lordosis. Psoas abscesses may cause psoas spasm with flexion of the hip.

Ford has emphasized that paralysis due to compression of the cord by epidural tuberculous tissue may be present without deformity of the spinal column, without muscle spasm and without demonstrable changes in the roentgenograms of the bones.

Involvement of the spinal cord is from pressure manifested only by weakness and stiffness of the legs without paraplegia or loss of control of the bladder. In instances of lesions below the lumbosacral enlargement paralysis if present is associated with atrophy, flaccidity and loss of reflexes

DIAGNOSIS The diagnosis is based on the presence of loss of weight, retarded growth, fever, changes in gait, altered posture and night cries, muscle spasm and limitation of movement, deformity of the spinal column, positive intracutaneous tuberculin reaction, and the roentgenographic changes in the spinal column In an occasional case there is paraplegia However, 8 of every 10 who have this sort of paraplegia recover in less than one year. In some recovery may be expected after several years.

Periostitis. Periostitis is an inflammation of the covering of the bone which occurs in both acute and chronic forms. Acute inflammation of the periosteum, like osteitis, occurs in association with various disease conditions of bone and as such cannot be definitely diagnosed except by means of roentgenologic examination, which reveals the characteristic increased density about the cortex of the bone.

Acute Periostitis. Acute periostitis follows either trauma, as in fracture or contusion, or infection, as in acute periostitis of the jaw secondary to dental infection. An acute periostitis is not uncommon as a complication of severe fevers.

There are local swelling, extreme pain, and heat. When sepsis is present, suppuration may follow. When the periostitis is of purely traumatic origin, the condition is usually transitory.

The diagnosis is usually easy if the etiology is known. Roentgenologic examinations will differentiate acute from chronic periostitis, since in the latter there will be evidence of bone formation.

active person in plaster casts an acute osteoporosis may arise. An acute osteoporosis is more likely to arise if the patient ingests large amounts of milk and if, in order to accelerate healing of the bone, vitamin D is administered. When the foregoing conditions prevail, the excessive amounts of calcium cause a hypercalcemia and hypercalciuria. The hypercalciuria is the cause of the formation of *renal stones* which occasionally occurs in patients who are in extensive casts. Renal stones seem to be of a higher incidence in those who have fractures of the pelvis and the femur. The formation of renal stones is less frequent in patients who have fractures of the upper extremity.

Anuria in a patient who has extensive immobilization of the skeleton occasionally occurs. If anuria does occur, the urine and the blood are examined for an excess of calcium. If there should be an excess of calcium, the removal of the cast may be a lifesaving measure

In such patients the high calcium content of the serum and the urine may give the impression of hyperparathyroidism. Hyperparathyroidism is a rare disease and its differentiation need not delay the removal of the cast.

Osteoporosis and the Senium (*Senile Osteoporosis*). A characteristic of senility is decreased intensity of protein synthesis manifested by atrophy of skin and muscles and by osteoporosis As the years advance beyond middle age, often the cortex of the bones of the whole skeleton shows signs of atrophy. The trabeculae of the cancellous bone become thinner and further apart, the greater part of the bone marrow becomes fatty, and only a few scattered islands of red bone marrow are in evidence In extreme examples of the disease the vertebrae collapse and the cortex of the other bones may become thin. This is the commonest form of osteoporosis. The skull and extremities are practically always free from osteoporotic involvement, except in the severest forms of the disease, and the lamina dura of the teeth remains normal. The vertebrae are the most profoundly affected

Osteoporosis and Vitamin C Deficiency. In children the commonest evidences of the lesions of scurvy are the irregular broadened epiphyseal line, the lateral spurs and occasional dislocation of the entire epiphysis, the decreased calcification behind the epiphyseal line, the thin diaphyseal cortex, and the rarefied shaft Normal calcification of bones and teeth seems to be dependent on adequate vitamin C. Ascorbic acid deficiency leads to decreased bone matrix formation and in turn to *osteoporosis.*

Adult Scurvy. Scurvy is rare in adults The bone lesions in the adult are limited to subperiosteal hemorrhages as described in infantile scurvy. Intracranial bleeding is spoken of, but it is not common in the adult

The history of deprivation of those foods which contain vitamin C is usually definite except when scurvy occurs during the course of chronic starvation. The concentration of vitamin C is decreased in the blood. Roentgenologic examination of the long bones may be diagnostic

Osteoporosis and Rickets. Rickets is a metabolic disease due to deficiency of vitamin D caused by insufficient exposure to sunlight which produces changes in the viscera, muscles and tendons The characteristic changes in the disease referable to the skeleton which take place at the periods when the skeleton is developing most rapidly (that is, during the first two years of life) extend through to the age of puberty

When there is insufficient absorption of calcium from the intestine, proteinic bone matrix is formed in the normal way but no calcium phosphate is available for deposition As the normal growth or wear and tear of the skeleton go on, there is not enough calcium for growth, or the lost calcium is not replaced, and decalcification or osteoporosis appears (see Chapter 22).

Osteoporosis and Osteomalacia. The reactions of the skeleton in rickets and osteomalacia are fundamentally identical. In both diseases the osseous trabeculae are surrounded by broad osteoid seams, and thus the definition of osteomalacia as

the same as those of syphilis. The bone lesions are benefited by specific treatment for syphilis. The diagnosis depends more on the age of the patient, who as a rule is much younger than one who has syphilitic bone disease It is well not to make a diagnosis of yaws of the bone unless the patient comes from an area in which the disease is *endemic*

Hydatid Disease. Hydatid disease of bone occurs in only a few of those who have hydatid infection The common sites affected are the vertebrae, the pelvis, the femur and the humerus. The vertebrae are the bones most frequently affected. The *spongy tissue of the vertebral bodies* is a favorite site when hydatid disease attacks a bone The infection, as with hydatid disease elsewhere, usually starts in childhood While it is confined to the bone, the growth of the hydatid is so slow that symptoms do not become evident before adult life. There are no symptoms until the destruc*tion of the bone leads to fracture or dislocation or until the hydatid cyst has erupted* from the bone and caused *pressure or swelling*.

The diagnosis of vertebral hydatid disease is uncertain The general condition of the patient is usually excellent Symptoms are due to fracture or subluxation of the affected vertebra or to pressure by extraosseous extensions, which may be confused with lipoma or cold abscess. Although vertebral hydatid disease has no pathognomonic roentgenologic signs, certain features, such as absence of periosteal reaction, minimal collapse, slight involvement of intervertebral spaces only, increased density of bone together with areas of destruction and involvement of contiguous ribs when a thoracic vertebra is affected, aid the roentgenologist in the interpretation of the roentgenogram.

METABOLIC DISEASES OF THE BONES

Metabolic diseases of the bones may arise during the course of malnutrition or as the result of deficiencies of vitamins

Albright has reasoned that the diet is of etiologic importance in the production and the maintenance of bone If there should be inadequate amounts of protein *ingested*, the osteoblasts would be deprived of the necessary strength to produce the *organic matrix* which is the first requisite for the formation of bone To the contrary, if there is an *increased availability of calcium and phosphorus* in the system as a result of a diet rich in these substances there would be a decrease in normal degree of resorption of bone However reasonable these assumptions are, there is no evidence that osteoporosis ever results from an inadequate diet in man.

Osteoporosis and Metabolic Disorders of the Bones. *Osteoporosis* is a disease of the bones characterized by increased porosity from widening of the haversian canals and absorption or lack of calcareous material. Osteoporosis occurs in many *and diverse conditions which permit a decreased* formation of proteinic bone matrix Osteoporosis can be caused by any condition in which the synthesis of protein is impaired. In such instances the calcium taken from the intestine cannot be used for normal bone repair because no bone matrix has been formed It therefore is excreted in the urine Thus, in the initial stages of osteoporosis, hypercalciuria is a frequent occurrence, and occasionally renal stones develop. Osteoporosis occurs frequently in prolonged *immobilization of bone*, in *metabolic disturbances* and *deficiency states*, in the *senium*, in *prolonged semistarvation*, in the *menopause* and in *Cushing's syndrome*.

Immobilization of Bones. The daily use of the skeleton requires a certain *amount of maintenance*. The maintenance of the skeleton is a function of the osteoblasts. During immobilization of the skeleton the normal stimuli for osteoblastic activity are not operative, less proteinic matrix is made by the osteoblasts, and thus *less bone* is formed. In time, often in a week or two, the limb in a plaster cast reveals atrophy of the soft parts and particularly atrophy of the bone.

In instances of immobilization of a large part of the skeleton of a previously

Polyostotic Fibrous Dysplasia. Polyostotic fibrous dysplasia in females is characterized by abnormalities of skin and bone and of endocrine function. The cutaneous lesions are brown, nonelevated, pigmented areas which tend to be on the same side as the osseous lesions. The osseous lesions on histologic examination reveal osteitis fibrosa.

SYMPTOMS. The first manifestation of the disease is a segmental distribution, roughly similar to that of the osseous lesions, of pigmented areas of skin which consist of small or large irregular café au lait spots These lesions are often first observed soon after birth and are similar in every respect to the forme fruste of Recklinghausen's disease.

The skeletal manifestations are varied. They may be without symptoms, their presence having been discovered accidentally on roentgenologic examination on account of a fracture The fracture is therefore not a true one but a pathologic fracture. The symptoms are often grouped according to the grouping of the osseous lesions; that is, there may be pains in one leg and foot, one arm and hand and headache.

The symptoms of hyperthyroidism may develop at an early age.

Female patients who have osteitis fibrosa disseminata often exhibit sexual precocity. Catamenia may be established irregularly at an early age; in some instances before the age of 5 years The breasts develop and pubic and axillary hair appears. Synchronous with the sexual precocity is an associated skeletal and somatic precocity. During childhood these patients grow rapidly and are large for their chronologic ages, but growth ends before a large size is attained, owing to early closure of the epiphyses

EXAMINATION. These children are large for their age. If adulthood has been obtained, the patient is short of stature. The pigmented areas are present over an extremity in which lesions and fractures of bones are present The forehead is often prominent As stated, in female patients the breasts are well developed, and pubic hair and axillary hair are present during childhood The thyroid gland often is easily palpable.

Involvement of the upper ends of the femora often results in outward bowing, which in the presence of the bone disease predisposes to recurring fractures and pseudarthroses

Roentgenologic examination reveals osseous lesions characteristic of polyostotic fibrous dysplasia These lesions are usually confined to one side of the body except in the skull, where there may be a bilateral thickening of the bones at the base with obliteration of the frontal and sphenoidal sinuses The bone age is greater than the normal or actual age of the patient

The basal metabolic rate is often increased. Serum calcium, serum phosphorus, and serum alkaline phosphatase are usually within normal limits of concentration In these precocious girls the values for 17-ketosteroid urinary excretion and follicle-stimulating hormone are within the range of values for adult menstruating women In boys or men who have the disease, hormone disturbances have not been described

DIAGNOSIS The history, the physical examination and the presence of extensive osseous lesions which show an increased density on roentgenologic examination are sufficient for a diagnosis

Postmenopausal Osteoporosis. Between the ages of 40 and 60 years osteoporosis occurs almost exclusively in women It has therefore been assumed that the osteoporosis which develops in the 40 to 60 year age group may well be closely related to postmenopausal (endocrine) processes.

The assumption that osteoporosis in women more than 45 years of age is related to the postmenopausal syndrome is based on the proved influence of estrogenic hormones

adult rickets is justified. In both conditions the osteoporosis as revealed by roentgenologic examination is definite and sometimes of an extensive degree.

ENDOCRINE DISTURBANCES OF BONE

Disorders of the endocrine glands may profoundly affect the formation and the maintenance of bones Of these hormonal disorders the work of Albright has revealed that hyperparathyroidism is the most spectacular example.

Osteitis Fibrosa Cystica of Hyperparathyroidism. This bone disease is characterized by severe bone pains; generalized osteitis fibrosa; skeletal softening, with spontaneous fractures, angular deformities of the bones, and cysts and cystic tumors of the bones. The tumors are often referred to as giant cell tumors. There are an increased concentration of calcium in the presence of decreased concentrations of inorganic phosphorus and an increased concentration of alkaline phosphatase in the serum. There is an increased urinary content of calcium and phosphorus. In these patients bilateral renal stones and disturbed renal function may be present. The disease occasionally is accompanied by muscular hypotonia, fatigue, polyuria, palpitations and dyspnea. Nausea and vomiting are common. The bone changes are easily demonstrated by roentgenographic examination.

On examination tumors may be found in the jaw, metacarpals, metatarsals and at the ends of long bones. Bone deformities include bending of the long bones, deformities of the pelvis similar to those seen in osteomalacia, and various deformities of the vertebrae. A result of the vertebral changes is a decrease of stature, a pigeon-breast deformity of the thorax, and a disappearance of the neck into the thorax. The bones in this disease are more brittle than in osteomalacia, and fracture rather than bend The patient may be first examined for a recent fracture

Diagnosis of osteitis fibrosa cystica can be established on roentgenologic examination by the presence of a generalized decalcification and the even ground-glass appearance of the skull, cysts and tumors. A cortical "cyst" is most suggestive of hyperparathyroidism. The teeth fail to show any decalcification and therefore contrast markedly with the decalcified bones of the face The diagnosis is confirmed by the presence of hypercalcemia, hypophosphatemia and excessive urinary excretion of calcium.

Secondary Hyperplasia of the Parathyroid Glands and Bone Disorders. In this condition the parathyroid glands respond to the abnormal calcium and phosphorus metabolism rather than initiate it

Secondary hyperplasia of the parathyroid glands most commonly occurs in osteomalacia and in multiple myeloma and occasionally in generalized malignant metastasis in the bones Secondary hyperplasia of the glands may occur in children and in adults who have chronic renal failure with acidosis. The renal lesion seems to be one of the lower nephron type The disease is much more frequently present in those who have congenital lesions of the kidneys and changes in the skeleton.

The bone lesions present under these circumstances consist of osteitis fibrosa and are designated as *renal osteodystrophy* Occasionally a certain amount of bone deposit is present around the bone trabeculae in those who have chronic uremia. Despite the occasional occurrence of osteoid zones, the designation of renal rickets is not considered desirable by Snapper. He objects to the term renal rickets, even in children and young adolescents who have chronic renal failure, when the closure of [illegible] those of rickets

[illegible] lure

are hypocalcemia, acidosis and usually hyperphosphatemia. In instances of extensive parathyroid hyperplasia the calcium of the serum is often normal or *low normal* It seems possible that the secondary hyperplasia of the parathyroid glands is responsible for the change from the original hypocalcemia to a normal calcemia.

The thickening of the cortical and spongy tissue in some typical places such as the skull, ribs, vertebrae and femora may be so pronounced that macroscopic inspection discloses no difference between the cortex and the spongiosa. The long bones are characteristically clubbed in shape.

The symptoms are variable There is a retardation in physical development, but mental symptoms may or may not be present. Often optic atrophy and blindness are the first symptoms. Repeated bone fractures are characteristic. The head may be enlarged, probably owing to the thickening of the cranial bones as well as to a slight hydrocephalus.

On roentgenologic examination, bands running parallel to the line of the epiphyses may be observed in the bones of the hands and feet and in the metaphyses when there are only moderate degrees of calcification. In the scapulae, the ossa ilii, and the tarsal and carpal bones these bands are ring-shaped.

Biochemical tests reveal no signs of hyperparathyroidism The blood has normal values for calcium, inorganic phosphorus and magnesium. There is a normal number of units for (alkaline) phosphatase. The cellular elements of the blood are normal in the early stages of the disease. The absence of anemia has been regarded as an argument in favor of the conception that the osseous anomalies of marble bone disease are primary and not dependent on the damage of the bone marrow.

In favor of the diagnosis of marble bones is the presence of atrophy of the optic nerve associated with the tendency to bone fractures, malformation of the thorax, the thickening of the lower end of the femur, the peculiar shape of the head and deformed or incomplete teeth.

Chalky Gout (Tophaceous Gout). Chalky gout is a form of calcinosis, according to Rosenberg, characterized by deposition of calcium salts in the terminal phalanges of the toes. The mechanism by means of which the calcium is deposited is unknown The calcium concretions consist of calcium phosphate and calcium carbonate which usually are present in the same proportion as in bone. Small amounts of magnesium carbonate and phosphate, cholesterol and fatty acids also have been found in the deposits.

For a discussion of calcinosis, see Calcium in Chapter 22

Osteitis Deformans (Paget's Disease). Sir James Paget wrote, in part, of osteitis deformans:

"It begins in middle age or later, is very slow in progress, may continue for many years without influence on the general health, and may give no other troubles than those which are due to the changes of shape, size, and direction of the diseased bones.

"The disease affects most frequently the long bones of the lower extremities and the skull, and is usually symmetrical The spine, by change in its own structures, may sink and seem to shorten with greatly increased dorsal and lumbar curves, the pelvis may become wide, the necks of the femora may become nearly horizontal, but the limbs, however misshapen, remain strong and fit to support the trunk

"In its earlier periods, and sometimes through all its course, the disease is attended with pains in the affected bones, pains widely various in severity and variously described as rheumatic, gouty, or neurologic, not especially nocturnal or periodical It is not attended with fever No characteristic conditions of urine or faeces have been found in it.

walls, and not only the walls of their shafts, but in a very characteristic manner, those of their articular surfaces

"The outer surface of the walls of the bones was irregularly and finely nodular, as with external deposits or outgrowths of bone, deeply grooved with channels for the larger periosteal blood-vessels, finely but visibly perforated in every part for transmission of the enlarged small vessels Everything seemed to indicate a greatly increased quantity of blood in the vessels of the bone."

on calcium metabolism. The decreased production of estrogens during the menopause may result in decreased osteoblastic stimulation.

The symptoms of postmenopausal osteoporosis develop slowly. However, in some, skeletal deformities with a marked loss of stature may be present. The first symptom is often a sharp pain in the back after slight trauma. On roentgenographic examination of the spinal column a marked decalcification, particularly of thoracic and lumbar portions, is apparent. Atrophy of the bone is often so advanced that only the end-plates of the vertebrae are denser than the intervertebral disks. In the lumbar region, where the pressure is greatest in the center of the vertebrae, the osteoporosis causes the formation of fish or hourglass vertebrae. The elastic intervertebral disks expand, at the expense of the softened vertebrae, and often become wider than the vertebrae themselves. Ultimately a complete collapse of one or more vertebrae may occur In less advanced instances there may be present herniation of the nucleus pulposus.

Patients who have postmenopausal osteoporosis often show remarkable improvement after administration of testosterone propionate. However, actual recalcification of the osteoporotic bones rarely is observed.

Osteoporosis in Cushing's Syndrome. Cushing's syndrome may result from cancer or adenoma of the adrenal cortex, unilateral or bilateral hyperplasia of the adrenal cortex, or basophilic adenoma of the pituitary gland

In Cushing's syndrome the error in protein metabolism results in an inadequate repair of tissue, manifested by atrophy of the muscular system and an insufficient formation of bone matrix, and consequently osteoporosis. The osteoporosis involves the spinal column, pelvis and ribs. The intervertebral disks compress the bony part of the spinal column, and fish or hourglass vertebrae develop in the lumbar portion, while wedging of vertebrae is prominent in the thoracic portion In the later stages of the disease actual compression fractures of the vertebrae occur In more advanced disease the skull and the long bones become osteoporotic. In the calvarium the decalcification is localized mainly in the frontal and parietal bones

In the differential diagnosis hyperparathyroidism with osteitis fibrosa cystica generalisata, lipoid granulomatosis (eosinophilic granuloma, Hand-Schuller-Christian disease, xanthomatosis), and Recklinghausen's neurofibromatosis are considered

In those who have extensive involvement of the skeleton, secondary lesions may arise which are incompatible with prolonged life. The thorax may be so deformed that cor pulmonale is inevitable Pathologic fractures are common and usually heal well with the exception of those at the upper ends of the femora The endocrine disorder may be benign The skeletal lesions are usually benign Often there is little or no progression for a long time in the extent of the skeletal involvement.

Hypothyroidism. A characteristic of juvenile hypothyroidism is a retardation in osseous development with a resulting subnormal bone age as determined by roentgenologic examination. In addition to the retarded development there may be some abnormal ossification of the cartilages of the epiphyses and of the round bones.

DISEASES OF THE BONES ASSOCIATED WITH BLOOD DYSCRASIAS

Changes in the femora, tibias, fibulas and cranium of almost specific configurations occur during the course of some of the blood diseases such as Cooley's anemia. Osteoporosis too may occur during the course of a chronic anemia (see Chapter 12).

DISEASES OF THE BONES OF UNKNOWN ETIOLOGY

Marble Bones (Osteopetrosis). The disease, sometimes called also ivory bones and Albers-Schönberg disease, is often of familial occurrence (about 40 per cent of the cases). It may be hereditary

Complicating fractures may result from trifling causes.

PSEUDOFRACTURES

Pseudofractures are transverse zones of rarefaction varying in width from less than 1 mm. to more than 1 cm., over which there is a thickening of the periosteum. Pseudofractures affect various portions of the skeletal system and often are symmetrically distributed. They are generally an indication of certain weaknesses or dysfunction of the skeletal system

There are no signs or symptoms which may be said to be characteristic of pseudofractures. Pain is the commonest complaint, and may be an ache or may be most noticeable when pressure is exerted over an affected region. This is accompanied by a degree of limitation of function due in part to the pain elicited and in part to the subjective sensation of giving way of the affected bone. When the leg and the pelvis are involved, there may be a waddling gait similar to that found in congenital dislocation of the hip and coxa vara The patient may have the greatest difficulty in climbing stairs or in rising from the sitting position, and may show a definite hesitation in beginning to walk The reflexes may be abnormal, as a result of the disturbances in prolonged dysfunction of the calcium-phosphorus metabolism

The diagnosis is made roentgenologically.

TUMORS OF THE BONES

Bone tumors are classified as benign or malignant neoplasias.

Benign Tumors. Meyerding classified benign bone tumors as follows: (1) osteoid osteoma, (2) benign osteogenic tumors which occur as (a) osteoma or exostosis and (b) chondroma, (3) benign fibroma; (4) benign giant cell tumors, (5) benign vascular tumors of bone (angioma) Also included in this category are the lymphangiomas and the fibrosis secondary to these processes; (6) bone cysts; and (7) epiphyseal chondromatous giant cell tumor (Codman's tumor)

1. ***Osteoid Osteoma.*** An osteoid osteoma is a small, benign neoplasm of bone consisting of osteoid tissues carried by a substratum of vascularized osteogenic connective tissue It occurs most frequently in boys and young men, but it may occur throughout middle age. The tumor is commonest in the tibia or femur but may occur in other parts of the skeleton The etiology is unknown

The first symptom is pain. In the beginning mild and vague, it progresses in severity and constancy and may be described as a boring, localized pain It is worse at night than during the day If the lesion is near a joint, there may be limping from the stiffness, and weakness and pain on even limited motion Often when the patient first consults a physician, the symptoms have been present for less than 6 months; sometimes, from 6 months to 2 years.

There is a localized tender point, and often a tumor in the painful area. Disuse atrophy of adjacent muscles and increase in joint fluid, simulating a primary arthritis, may be present.

The clinical diagnosis is made on the basis of roentgenographic examination. The final diagnosis is established by histologic examination of the tissue obtained by biopsy or that removed at the time of operation

Osteoid osteoma is to be distinguished from solitary abscess, sterile abscess of Brodie, sclerosing nonsuppurative osteomyelitis, and syphilitic or tuberculous osteitis.

2. ***Benign Osteogenic Tumors*** (a) ***Osteochondroma*** (*Osteoma Exostosis*) An osteochondroma is a bony skeletal outgrowth with a cartilaginous cap. The tumor occurs most frequently in boys and in men less than 25 years of age The tumors arise near the ends of long bones at sites of tendinous attachments The growth is outward in the direction of muscle These are usually congenital tumors

ETIOLOGY. The etiology, as stated by Paget, is unknown. The disease is one of advanced life, setting in at any time after the age of 30 years.

PATHOLOGY. There is little to be added to the description of the pathology as this was originally made The gross changes consist of a general thickening and bowing of the long bones, both characteristics being in evidence throughout the shaft and in advanced stages involving the epiphyses as well. Not infrequently the bone is increased to twice its normal size. In all cases the bowing is in the nature of an accentuation of the normal curve together with a moderate degree of torsion. Actual lengthening also takes place. The normal ridges and prominences may be the first to show the hypertrophy. The normal markings of the bone are lost The outline is fairly regular but the surface is uneven and is broken by rather large osteophytic outgrowths. These modifications are particularly common to the tibia, femur, fibula, pelvis, humerus, radius, ulna and clavicle The skull is thickened in some cases to two or more times its normal thickness.

SYMPTOMS. The onset is insidious, the progress is gradual. The patient may be scarcely conscious of the disorder until his attention is directed toward the deformities by his family. The first symptom in some instances is pain. If there is no pain, medical advice is not sought until very late in the course of the disease.

The pain most commonly is situated in the legs over the front of one or both tibias and is dull and felt deep in the bones It occurs in all possible grades, from mere discomfort to actual paroxysms of lancinating character. It is worse at the end of the day or at night and especially after long standing and unusual fatigue. Pains in the skull are rare. Pain may be absent throughout the course of the disease. One of the most constant and severe symptoms is cramps in the muscles of the legs.

EXAMINATION. The muscles of the legs or arms, if the bone is affected, show atrophy and occasionally edema. Tenderness to pressure over the muscles may be present.

The most pronounced deformities are to be found in the legs No other condition except rickets in children gives such an extreme degree of curvature of the legs. So great may the bowing become that the legs are crossed and walking is almost impossible. The sensations and reflexes are normal.

The head appears enormous and seems to rest directly on the shoulders. The enlargement is confined to the calvarium, which is symmetric but has a tendency to irregularities of the surface. Especially great hypertrophy of the supra-orbital portion of the frontal bone and the malar processes gives to the skull a massive appearance

The trunk often appears small and the thorax is compressed laterally Immense increase of the anteroposterior diameter accompanies the decrease in the lateral diameter The whole thorax is rigid and in consequence the respiration is mainly diaphragmatic The scapulas may show similar changes The spinal column becomes bowed, with the most marked curve in the thoracic portion, and finally complete rigidity develops. The bones of the upper extremities seldom show very noticeable alterations. The pelvis is very broad and massive with abnormal flaring of the iliac crests.

DIAGNOSIS' The diagnosis can be made in the advanced instances of the disease from the history and examination. However, the diagnosis is usually made by the roentgenologist from films made for causes other than bone diseases. The disease thus is often discovered before there are symptoms. When the disease is progressing rapidly there is increased concentration of calcium and of phosphates in the urine. The serum phosphatase is greatly increased in Paget's disease. The effect of immobilization results in a decrease of the alkaline phosphatase in the serum and the ... d phosphates in the urine

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5. ***Vascular Neoplasms of Bone. Benign Angioma.*** (a) *Hemangioma* may form in periosteum or marrow, usually in vertebrae or skull or in soft tissue where it may cause bone destruction. The tumor occurs in young adults and has no sex preference. It may be present, particularly if situated in a vertebra, in middle-aged patients.

Often there are no symptoms. When a hemangioma is situated in a vertebra, pain may be localized or may extend to the anterior part of the thorax, abdomen or down the leg

The clinical diagnosis is made on the basis of roentgenographic examination. The final diagnosis is made on the basis of histologic examination of the tissue obtained for biopsy or that removed at the time of operation The preferred treatment is irradiation when lesions are inaccessible (as in vertebral bodies) or too large to excise.

(b) *Lymphangioma* was recorded by Bickel and Broders as causing almost complete destruction of the ilium from the sacro-iliac joint to the acetabular region. These lesions occur in the vertebrae. They may occur in other bones.

6. ***Bone Cyst.*** Bone cyst occurs most frequently in the metaphyseal regions of long bones, particularly in the upper ends of the humerus and the femur; these account for about half of the cases Other bones involved are the distal part of the radius, proximal part of the fibula, distal part of the ulna, and the phalanges of the hand or foot, ribs, pubis and ischium Latent bone cysts, recognized in adult life, may be present in the middle third of the shaft of the humerus and the femur. Bone cysts are commoner in boys and young men than in older men or in women They may be present in middle-aged patients.

Often there are no symptoms. When symptoms are present, they consist of mild pain, usually felt after prolonged use or strain of the part. A pathologic fracture may be the first manifestation. Trivial injury causing fracture of a long bone near a joint suggests the presence of a bone cyst.

A swelling may be palpated in the upper part of the tibia or in the lower part of the radius and ulna.

The clinical diagnosis is made on the basis of roentgenographic examination The final diagnosis is made on the basis of histologic examination of the tissue obtained for biopsy or that removed at the time of operation

Healing of the pathologic fracture may heal the cyst.

7. ***Epiphyseal Chondromatous Giant Cell Tumor*** (*Codman's Tumor*) This tumor occurs in the upper end of the humerus in the region of the tuberosities, in the lower part of the femur, upper part of the tibia, and in the metacarpal and astragalus bones, more commonly in boys and young men than in older men or in women. The lesion is said to arise in the epiphysis and extend into the neighboring metaphysis, but it is never situated exclusively in the metaphysis

Pain, occasionally swelling, and limited motion in the adjacent joint are the symptoms There may be tumor at the site of pain.

The clinical diagnosis is made on the basis of roentgenographic examination The final diagnosis is made on the basis of histologic examination of the tissue obtained for biopsy or that removed at the time of operation

Malignant T[illegible] [illegible]
diverse compone[illegible]
osteoblastic or [illegible]
sarcoma Those arising from the connective tissue of the bones are fibrosarcoma; from the cartilage, chondrosarcoma, from the vessels, hemangio-endothelioma; from the bone marrow, myeloma Those arising from the reticuloendothelial cells are termed either reticulum cell sarcoma or lymphosarcoma; and those from fat are liposarcoma

Osteogenic Sarcoma. Osteogenic sarcomas are complex structures. Only the well-trained histologist can differentiate between the various types of these tumors. The histologists cannot always agree among themselves on the diagnosis of the same histologic specimen.

There are often stiffness and limping which may have been present from 1 to 4 years. A bursitis may be the presenting symptom. Acute symptoms of pain, swelling and vascular compression may be due to an increased growth incident to malignant change.

Inspection and palpation reveal a firm, painless, bulging juxta-articular mass over which soft tissues move freely. Pain and fluctuation may be found with bursitis

The clinical diagnosis is established by roentgenographic examination. The final diagnosis is established by histologic examination of the tissue removed for biopsy or that removed at the time of operation.

(b) **Chondroma.** Chondromas occur in the small bones of the hands and feet, spinal column, pelvis, ribs and sternum in patients from the age of 10 to 30 years.

Rickets, trauma, differentiation of prechondral connective tissue or cartilage cells, and supernumerary joint cartilages derived from prechondral connective tissue are some of the possible etiologic causes

The tumors may become large before symptoms appear However, after tumor formation there may be aching pain, deformity and, frequently, pathologic fractures The tumors may be present for years without causing symptoms.

The clinical diagnosis is made on the basis of roentgenographic examination. The final diagnosis is established by histologic examination of the tissue obtained for biopsy or that removed at the time of operation

3 ***Fibroblastic Tumor. Benign Fibroma.*** Benign fibroma, or nonosteogenic fibroma of bone, occurs in the shaft of a long bone, usually with 1 or 2 inches (about 2 5 or 5 cm) of unaffected shaft between the lesion and the nearer epiphyseal plate. These tumors may occur at any age or in either sex

Often there are no symptoms However, there may be tenderness and swelling with pain and stiffness in the adjacent joint

The clinical diagnosis is made on the basis of roentgenographic examination The final diagnosis is established by histologic examination of the tissue obtained for biopsy or that removed at the time of operation.

4. ***Giant Cell Tumors*** *(Osteoclastoma)* Benign giant cell tumors occur in long bones, principally in the tibia, femur or radius They arise in the epiphysis and progressively invade cancellous bone They occasionally present eccentrically and are called subperiosteal giant cell tumors Growth is limited by periosteum and articular cartilage They occur from the age of 10 to 40 years and have no sex preference

Trauma seems to be important There is subcortical or subperiosteal hemorrhage with subsequent atypical repair of avascular cortical bone

Pain may begin as an intermittent, mild, dull ache made worse by activity and diminishing or disappearing during rest Swelling is often present but it is not an early symptom When there are marked expansion and destruction of bone, there is pain Movement of the adjacent joint may be limited

Palpation often elicits tumor and tenderness. Pathologic fractures are common These fractures are suggested by sudden pain, altered contour and increased swelling. Recurrences after operation occur. Malignant degeneration was present in 19 per cent of Meyerding's patients

The clinical diagnosis is made on the basis of roentgenographic examination. The final diagnosis is made on the basis of histologic examination of the tissue obtained for biopsy or that removed at the time of operation.

Bone cysts occur in the diaphysis before the adjacent epiphysis closes and are to be differentiated from benign chondroblastoma; from the lesions of hyperparathyroid disease of bone, which occur in the shaft, are multiple, and are associated with altered blood chemical findings; and from central chondroma, myeloma and medullary osteolytic type of osteogenic sarcoma.

Accessible lesions are treated surgically. There are many physicians, however, who advocate primary irradiation, believing that better function is maintained and operation avoided.

The clinical diagnosis is made on the basis of roentgenographic examination. The final diagnosis is made on the basis of histologic examination of the tissue obtained for biopsy or that removed at the time of operation.

The prognosis is always grave; only 15 per cent of patients live 5 years The usual course in the fatal instances averages about 14 to 15 months. Those patients usually receive surgical treatment.

2. ***Secondary Chondrosarcoma.*** This cartilaginous malignant tumor originates in a benign lesion. The benign tumors thus affected include cartilaginous exostosis, central chondroma, hereditary deforming dyschondroplasia and Paget's osteitis deformans

Secondary chondrosarcoma occurs more frequently in men between the ages of 35 and 55 years than in men of other ages or in women. The most frequent sites of occurrence are the lower end of the femur and upper end of the humerus. The tumors may appear about the ribs, in the region of the heel, or in the pelvis

There is a history of an injury, a swelling which has persisted, or the patient may state that there has always been a deformity in the region in question After a number of years the swelling increases in size and pain is present A pathologic fracture occurs occasionally.

Aside from the presence of the tumor, and perhaps some limitation of the adjacent joint, the results of examination are negative

The clinical diagnosis is made on the basis of roentgenographic examination. The final diagnosis is made on the basis of histologic examination of the tissue obtained for biopsy or that removed at the time of operation

The life expectancy after the development of a secondary chondrosarcoma varies from 2 to 10 years The majority of patients who have been reported as cured have been treated by radical resection or amputation and not by curettage, cauterization or roentgen rays.

Endothelioma (*Ewing's Tumor*). The nature of this tumor is strongly suggestive of an infection The patient exhibits a generalized systemic reaction with fever and leukocytosis The histologic appearance is said to resemble that of an inflammatory lesion The disease is largely limited to the white races though it has been recorded in Negroes. There is a preponderance of incidence among males.

The tumor occurs most commonly in the femur and the tibia, and elsewhere in the following order of frequency in the pelvis and ribs, the clavicle, scapula, humerus, radius and ulna, lumbar and cervical vertebrae and the skull.

The symptoms commence with pain which is variable in intensity, usually intermittent, becomes increasingly more severe, and is commonly worse at night than during the day. The lump or swelling in Ewing's tumor is present by the time there is pain, and in about one fourth of the cases may be present before there is pain. Fever is a common symptom and is of the intermittent spiking type. The temperature is usually of the range between 99 and 101 F (37.2 and 38 3 C).

Spontaneous remissions occur with a decrease in the size of the tumor, less pain, and lack of fever, only for the symptoms to return again In some cases the course is rapid The average life expectancy is less than 2 years

In a few of those who have this tumor the symptoms may have been such that the patients are operated on for incision and drainage of abscesses

The swelling is tender, usually fusiform in shape, and further mimics an infection with increased local heat and dilated overlying veins. These tumors are further removed from the articulations than many other bone tumors and hence the disability is a less constant feature as an early symptom.

Leukocytosis is fairly constant; the leukocyte count is in the range from 10,000 to 20,000 per cubic millimeter of blood The differential blood count is not characteristic, it is not unusual in any way. Anemia is not an early finding Endothelioma metastasizes to other bones, to the lungs and to the lymph nodes and viscera.

The clinical diagnosis is made on the basis of roentgenographic examination.

Osteogenic sarcoma is essentially a disease of youth, the majority of the patients being less than 30 years of age. The tumor occurs more commonly in females than in males.

Osteogenic sarcoma characteristically is situated in the lower extremity in the region of the knee. However, it may occur in the metaphyseal ends of any of the long bones It does not occur in the shaft or the epiphysis.

Pain is the first symptom. In the beginning it may be intermittent or transient. As the tumor enlarges, the pain is continuous, boring, persisting, and worse at night than during the day.

The tumor is usually ill-defined and diffuse in the early stages; later there is a definite mass firmly attached to the underlying bone. The consistency varies greatly, depending on the type of sarcoma. The sclerosing osteogenic sarcoma is characteristically of bony hardness; the osteolytic type is less firm in texture.

As the tumor increases in size, the skin becomes shiny and stretched. Often there may be dilated veins in the region of the tumor and an increased surface temperature Increased heat of the tumor is often observed, especially in the more rapidly growing types.

Disability is produced by limitation of motion of the adjacent joint as the result of pain and tumefaction, but there is no actual involvement of the joint.

Leukocytosis and some fever may be present. The concentration of alkaline phosphatase in the blood serum is increased

The clinical diagnosis is established by roentgenographic examination The final diagnosis is made on the basis of histologic examination of the tissue obtained for biopsy or that removed at the time of operation.

The five-year survival rates run consistently between 15 and 25 per cent. The prognosis in general is much poorer in young children than in older persons.

In general most orthopedists agree that amputation is the only treatment in attempting a cure and that all other methods are adjuncts or palliative

Fibrosarcoma. This tumor arises from the nearby soft tissues or possibly from the connective tissue structures of the periosteum. The femur and tibia are the commonest sites. The upper extremity is involved to a less extent than the lower extremity The skull and pelvis may be involved.

Fibrosarcoma occurs infrequently. It tends to affect adults who are more than 30 years old

The first symptom is pain, which develops slowly over months. As time passes, there is a swelling and then limitation of movement of the affected part The swelling is deep, attached to the underlying bone, and most commonly is of a semisolid consistency Occasionally, but a distinctive feature when present, the tumor will cross a joint and involve a second bone. The lymph nodes may be enlarged These tumors metastasize by the blood stream, usually to the lungs.

The clinical diagnosis is made on the basis of roentgenographic examination. The final diagnosis is established by histologic examination of the tissue obtained for biopsy or that removed at the time of operation.

The prognosis of this tumor is better than that of the osteogenic sarcoma. The tumor is radioresistant. Surgical removal is the preferred treatment

Chondrosarcoma. Some chondrosarcomas are benign, while others are known to be malignant from the start and are called primary chondrosarcoma or chondroblastoma

1. ***Primary Chondrosarcoma.*** The primary chondrosarcoma occurs in young persons less than 30 years of age, with the greatest incidence in patients between the ages of 14 and 21 years. The sex ratio is about the same as in the osteogenic sarcomas; that is, 2 males to each female.

The commonest situations are the lower end of the femur, upper end of the tibia or upper end of the humerus' The symptoms and the findings on examination are the same as those of osteogenic sarcoma.

The leukocyte count is normal. True myeloma cells may be present. Numerous plasma cells may be observed and if so the disease may be termed a plasma cell leukemia. The platelet count is usually normal. Failure of the clot to retract and difficulty in obtaining serum are often experienced by the laboratory technician Viscosity of the blood is often greatly increased. The concentration of plasma protein may exceed 10 0 gm. per 100 ml The increase is due mainly to the globulin fraction, and the albumin-globulin ratio is reversed.

The serum in multiple myeloma may be anticomplementary. The concentration of serum calcium is often increased (12 to 16 mg. per 100 ml.) but, in contrast to the finding in generalized osteitis fibrosa cystica (except in the terminal stages when renal failure is extreme), the inorganic serum phosphorus is normal in amount or may even be increased The uric acid content of the blood may be increased to 25 or 30 mg per 100 ml

The urine often contains albumin and casts Bence Jones protein appears in the urine occurring in 6 of each 10 who have multiple myeloma It should not be regarded as characteristic of multiple myeloma, for Bence Jones protein occasionally *occurs in the urine of leukemic patients and polycythemic patients and in those who* have diffuse metastasis to the ribs; for instance, in carcinoma of the thyroid gland. The consensus is that the excretion of Bence Jones bodies in the urine is specific for some pathologic process situated in the bones that contain red marrow. In the presence of very high concentrations of serum proteins, the Bence Jones protein may be absent from the urine owing to an inability of the kidney to excrete it. A failure to concentrate the urine and retention of nitrogen may develop.

The *bone marrow* contains myeloma cells

The diagnosis is made on the basis of (1) the presence of Bence Jones bodies in the urine, (2) the roentgenologist's report of myeloma or metastasis, (3) increased plasma proteins (8 gm or more per 100 ml of blood), (4) difficulty encountered in making of the blood smears—rouleaux formation of the erythrocytes Despite the prolonged course, the prognosis is ultimately unfavorable

Reticulum Cell Sarcoma. Reticulum cell sarcoma is considered a primary bone tumor in that it arises from the parts of the reticuloendothelial system which are found in bone It may resemble histologically an ordinary reticulum cell lymphosarcoma which has metastasized to bone

This tumor has been considered to be the same as Ewing's sarcoma It occurs in an older age group than Ewing's tumor, however, being found in early adulthood. It occurs more frequently in men than in women

Reticulum cell sarcoma occurs primarily in the metaphyseal regions of the long bones but may involve the flat bones also

Pain is the primary symptom A tumor which is tender may be present. There is no fever, nor is there leukocytosis.

The clinical diagnosis is made on the basis of roentgenographic examination The final diagnosis is made on the basis of histologic examination of the tissue obtained for biopsy or that removed at the time of operation The outlook is more favorable than in Ewing's tumor This tumor is radiosensitive

Liposarcoma. The revised bone sarcoma registry of the American College of Surgeons includes liposarcoma as a malignant tumor which may be primary in bone This tumor is rare

The tumor is commonly found in the soft tissues Its existence as a primary tumor of bone is doubtful Liposarcoma of bone, as well as of any other part of the body, tends toward multiple lesions

The clinical diagnosis is made on the basis of roentgenographic examination. The final diagnosis depends on findings on histologic examination of the tissue obtained for biopsy or that removed at the time of operation

Secondary Malignancy of Bones (Carcinoma). Metastatic malignancy to the bone is carcinoma from organs and tissue of epidermal origin, such as the digestive

The final diagnosis is made on the basis of histologic examination of the tissue obtained for biopsy or that removed at the time of operation.

An outstanding feature of Ewing's tumor is that the original lesion responds to roentgen therapy. Despite the radiosensitivity of the primary lesion, metastatic lesions nearly always develop and they are usually more resistant to treatment than the primary lesion. Surgical treatment offers no better prognosis than does roentgen therapy.

Multiple Myeloma. Myeloma involves the bones of the skeletal trunk, producing pain and resulting in pathologic fractures and anemia. The disease is often distinguished by the excretion of Bence Jones protein in the urine and its accumulation in the blood However, the presence of Bence Jones protein in the urine is not diagnostic, for it does not occur in the urine in more than 6 of each 10 who have the disease

The etiology of multiple myeloma is unknown. The disease often appears after the age of 40 years It is at least twice as frequent in men as in women.

Pain, tumors, deformity, pathologic fractures and neuralgic or neurologic symptoms are the commonest complaints, and one of these may be the basis of the presenting complaint Less frequently, complaints referable to anemia or abnormal bleeding or symptoms suggesting nephritis come first.

The *pain* is wandering and intermittent, and it is referred to the back, less often to the thorax or the extremities. Girdle sensations, or extension down the legs may be present Generally the onset of pain is related to motion or pressure. The pain may be extremely severe and may last for hours or days but intermittency and even remissions for several months are common The disease is often accidentally discovered by finding the Bence Jones protein in the urine or by evidence revealed in roentgenograms made for other diagnostic purposes.

Gastrointestinal symptoms are rare but have been described as diarrhea, colicky pains, nausea and vomiting Hematemesis and melena have been described Epistaxis may occur and ecchymosis, bleeding about the gums and lips, and petechiae may be present in some of these patients.

Intravascular thrombosis may occur. Chronic bronchitis and pulmonary emphysema are common complications of the thoracic deformity in aging patients but are not symptomatic of multiple myeloma The liver, spleen and lymph nodes are not enlarged

There may be evidences of loss of body weight. The tumors are multiple and usually confined to the ribs, sternum, spinal column, clavicles, skull, or to the extremities about the shoulder girdle or the pelvic girdle Generally the swellings are small, the larger ones not more than a few centimeters in diameter. The tumors are elastic, often yielding a distinct crepitation on palpation. Single palpable lesions may occur, but the roentgenogram will reveal the presence of more than the one palpated. Pathologic fractures are frequently present and discovered on roentgenographic examination Thoracic deformity is common

Paraplegia due to compression of the spinal cord, intercostal neuralgia, radiculitis, diplopia, anisocoria and failing vision, or complete blindness due to thrombosis of the central artery of the retina, as well as other neurologic syndromes, may be observed with multiple myeloma as their cause.

Extra-osseous tumors may be present in the testis or in the tonsil Pain in these tumors is absent if the skeleton is not involved.

Anemia is of only a moderate degree if present at all Enumeration of the erythrocytes is difficult, owing to clumping The clumping of the erythrocytes is related to the increased quantity of globulin in the plasma which causes a marked tendency to clumping and to rouleaux formation. Clumping and rouleaux formation may prevent the making of satisfactory blood smears. Blood grouping may be difficult and the serum may need to be warmed or diluted before a satisfactory test can be made. Of course, the sedimentation rate of the erythrocytes is increased.

and postoperative convalescence. It seems that irrespective of the changes in the blood or the vessel walls the essential element in the production of arterial thrombosis is slowing of the blood flow.

SYMPTOMS. Numbness, coldness and tingling, and loss of muscular power of the affected extremity are the most constant symptoms. Pain is inconstant in sudden arterial occlusion. It is present in only one half of those patients who have this misfortune. Pain when present is usually severe.

As has been stated, sudden arterial occlusions often occur during the course of a severe illness The general symptoms of the primary disease may mask those of the vascular accident. If the primary disease is mild, a sudden arterial occlusion may be manifested by tachycardia, profuse perspiration, and anxiety and pain.

EXAMINATION. There is absence of a pulse in the artery distal to the occlusion. There are coldness, a partial loss of sensation, and for a short time after the occlusion, vasodilatation

After a sudden arterial occlusion there may be present gangrene or ischemic neuritis. When a large artery, such as the femoral, is affected, usually an extensive gangrene ensues which involves the leg and the foot In instances in which the lower part of the aorta is involved, there are severe pain and complete ischemia and paralysis of one leg or [illegible]
the lower extremity by [illegible]
may involve digits only [illegible]
followed by ischemic neuritis or a state of chronic arterial insufficiency Subsequent arterial occlusions are to be expected

Ischemic neuritis is common among diabetic patients, and it may merge with the so-called true diabetic neuritis Ischemic neuritis occurs most commonly when the occlusion is nearer the aorta The pain of ischemic neuritis, like pretrophic pain, results from a lack of blood flow to the part It is characterized by having the distribution of the peripheral nerves It may occur with or without ulceration or gangrene. If there is ulceration or gangrene present, the pain of ischemic neuritis extends proximally from these processes Muscular weaknesses and reflex disturbances may follow the ischemic neuritis

DIAGNOSIS. A cold pulseless extremity is diagnostically a definite entity.

The prognosis as to life is poor when simple arterial thrombosis develops in the arteries of the extremities in the course of infectious diseases or congestive heart failure.

Traumatic Arterial Thrombosis. Penetrating wounds and severe blunt trauma may result in bruising or crushing of the wall of the artery with subsequent thrombosis. The prolonged use of a crutch may cause thrombosis of the axillary or brachial artery. Cervical ribs have caused thrombosis of the subclavian artery. The symptoms and findings of acute traumatic arterial thrombosis are those of acute arterial occlusion.

Arteriosclerosis and Arteriosclerosis Obliterans. ***Arteriosclerosis.*** The etiology of arteriosclerosis is not known The consensus is that the mechanical theory and the metabolic theory are the outstanding ones in regard to the cause and development of arteriosclerosis

The advocates of the mechanical theory see the arteries change in texture as the result of continual pulsations as the years pass This change in the texture of the arteries constitutes arteriosclerosis, which reaches its most extensive development in old age. The mechanical theory is not hampered by the fact that manifestation may begin in young [illegible]

The metabolic theory of the development of arteriosclerosis is based on defects in lipoid metabolism It is assumed that if atheromas contain quantities of lipoid material, [illegible]bolism is at fault This theory does not seem to be hampered by the fact

tube and endocrine glands. These malignant metastases are described in various parts of this book in the descriptions of the organs affected by the primary malignant focus. Sarcomatous metastasis to bone is less frequent.

DISEASES OF PERIPHERAL VESSELS AS THEY AFFECT THE EXTREMITIES, OTHER PARTS OF THE BODY AND LOCOMOTION

Anomalies of Peripheral Blood Vessels. Anomalous situations of peripheral blood vessels are often present, and these seem to originate from the choice of unusual paths selected by the developing primitive vascular plexuses. Other reasons for abnormally situated vessels may be the persistence of vessels which are normally obliterated, and the disappearance of vessels which normally persist Incomplete development fusions and absorptions of parts, usually distinct, may add to the difficulty in trying to find a peripheral pulsation which ordinarily has a definite situation.

Manifestations of Diseases of Peripheral Blood Vessels The presence of disturbances of the peripheral circulation is often made known by pain which is induced by exercise and relieved by rest, influenced by posture, localized to one digit or to a part or all of an extremity Often the pain is accompanied by color changes, and both are paroxysmal in occurrence and are influenced by elevation and dependency of the part Excessive cold or warmth of extremities together with abnormal pulsations in the arteries or enlarged veins may accompany the color changes and pain There may be present ulceration, gangrene, scleroderma, impaired nail growth, excessive calluses or paronychial infections and an enlargement or a smallness of extremities

The examination of the extremities of patients who are suspected of having peripheral vascular disease can be performed quickly The examiner, according to Allen, Barker and Hines, must answer the following questions in order to complete the examination. (1) Is swelling, atrophy, elongation or shortening of the limbs present? (2) Is ulceration, gangrene, scleroderma, eczema, varices or thrombophlebitis present? (3) Is the temperature of the skin abnormal? (4) Is the color of the skin abnormal? Do elevation and dependency of the extremities cause unusual discoloration of the skin? (5) Are pulsations in the peripheral arteries impaired? (6) Is there auscultatory evidence of arteriovenous fistula or aneurysm? If the answer to all these questions is "No," all peripheral vascular disease except Raynaud's disease and erythermalgia may be excluded. If the answer to any of these questions is "Yes," more detailed examination and analysis may be advisable

The more technical and detailed examinations comprise (1) tests of capacity of blood flow (vascular function tests) in skin as shown by vasodilatation, by reflex heat, artificial fever, anesthesia (local, general, spinal, and paravertebral), intradermal histamine and saline injections, and reactive hyperemia, (2) tests of capacity for blood flow (vascular function tests) in muscle, by walking certain distances and by ergographic measurements of muscle fatigue, and (3) test of the functional state of the vessels, by oscillometry and roentgenologic studies, especially by diodrast injection of arteries or veins Judgment, much experience and common sense are needed for proper appraisal of these special tests.

Arterial Thrombosis. *Simple Arterial Thrombosis.* In an occasional instance an occlusion of a peripheral artery may occur in the absence of disease of the endothelium of the artery and without a history of injury of the vessel. There is no evident source of the arterial embolus In those who have such an arterial occlusion, often there is a slowing of the blood flow, or a change in the contents of the blood, or both may be present.

The blood flow is slowed during starvation, severe infections and in polycythemia vera and at times in minor degrees of arteriosclerosis, congestive failure in heart disease,

arterial insufficiency; within 30 seconds, a marked degree; and within more than 60 seconds, an extreme degree.

In arteriosclerosis obliterans there are more or less constantly the following findings: a lower skin temperature of the foot or toes than of other parts of the body, often scarring and shrinkage of the digits, impairment of nail growth; paronychias which heal slowly, and ultimately may develop into gangrenous or ulcerative lesions often involving the bone of the affected digit.

Ulceration and gangrene of arteriosclerosis obliterans are of the dry type and are accompanied by little or no systemic reaction. When diabetes is present, the lesions may be of the moist type and there may be considerable systemic reaction with rapid development of lymphangitis and often septicemia.

In advanced stages of arteriosclerosis obliterans there is atrophy of the muscles of the leg, absence of subcutaneous fat, atrophy of the skin, and often osteoporosis.

Roentgenograms are of definite value in the distinction of arteriosclerosis obliterans from other types of occlusive arterial disease. Roentgenograms are made of the leg, the thigh and pelvis, and often lateral views of the lumbar region are taken to detect calcified arteries However, calcified arteries which are revealed by roentgenographic examinations may not prove or indicate occlusive vascular disease.

DIAGNOSIS. Intermittent claudication is almost pathognomonic of occlusive arterial disease, but it is not always present

The diagnosis of arteriosclerosis obliterans is made on the basis of the absence of pulsations in one or both of the posterior tibial or popliteal arteries and unequal postural color changes in the two extremities. The presence of all of the other symptoms and findings is confirmatory evidence of the disease. Roentgenologic examination may reveal visible calcification in the walls of the vessels.

In general, arteriosclerosis obliterans is a progressive, degenerative vascular disease.

Thromboangiitis Obliterans (Buerger's Disease) Thromboangiitis obliterans is a segmental, inflammatory, obliterative disease of the arteries and veins of the extremities of young men In rare instances the disease may affect the viscera

Thromboangiitis obliterans resembles an inflammatory vascular disease. The consensus is that the use of tobacco is an important etiologic factor

The lesion of thromboangiitis obliterans is a segmental, inflammatory, nonsuppurative panarteritis or panphlebitis with associated thrombosis without necrosis of the wall of the vessels

SYMPTOMS Intermittent claudication is the first symptom in more than 7 of every 10 who have the disease Once intermittent claudication is present, it will remain present for the remainder of the life of the patient It occurs most commonly in the arch of the foot or in the calf of the leg distal to a point of demonstrable arterial occlusion Intermittent claudication is an ache, sense of fatigue, persistent cramp or severe aching, squeezing pain It occurs only after exercise of the affected muscles and is relieved promptly by rest without change of position.

Often as a first symptom some of the digits of a foot or hand may feel abnormally cold on short exposure to a cold environment. Often there is an associated sensation of numbness or other paresthesias

Pretrophic or rest pain may persist for hours, it is more severe at night than in the daytime and may be premonitory of ulceration or gangrene. The pain of ischemic neuritis is severe, paroxysmal and widespread, and is associated with various paresthesias The pain of ulceration and gangrene is localized and is situated in the region adjacent to ulcers or gangrenous tissue The pain of osteoporosis and atrophy is associated with weight bearing or pressure

The lesions of superficial thrombophlebitis, which occur in thromboangiitis obliterans, are usually painful but the pain is not severe. It persists until the lesion involutes, and then gradually disappears

that although extensive arteriosclerosis increases with age, there is a tendency to a decrease of concentration of blood lipoids as age advances

Disorders of lipoid metabolism manifested by lipemia often are accompanied by severe atherosclerosis The presence of diabetes mellitus is accepted as a predisposing factor to severe and premature arteriosclerosis, atherosclerosis and arteriosclerosis obliterans

Arteriosclerosis Obliterans. Arteriosclerosis obliterans, as it occurs in the extremities, is the result of an obstruction of the blood flow through large arteries to a sufficient degree to result in ischemia of the tissues of the extremities. A slowly developing occlusion may be better compensated for than the rapidly developing ones

SYMPTOMS In a slowly developing arteriosclerosis like arteriosclerosis obliterans intermittent claudication is the first symptom. The pain may be present in one leg or both legs, for instance in the foot, in the calf or in the thigh, and occasionally in the hips and lower part of the back. In the majority of patients, however, claudication is present only in the calf muscles. The pain of claudication requires fatigue for its development. The pain appears while the patient is walking. It is sharp and shooting, darting, moving rapidly lengthwise of a group of muscles. The pain increases in severity with the continuation of walking. Rest affords prompt relief Immediately on relief of the pain exercise may be resumed. The distance that the patient is able to walk before the distress develops varies with the proximity of the arterial occlusion to the aorta The distance may vary from 20 to 25 steps to a mile or more If the pain of claudication is not yielded to, there is a gradual stiffening and tightening of the muscles which, when the disease is severe, may reach the point that the patient is unable to use the part because of muscle spasms which are too painful to be endured. After claudication there may be soreness, tenderness and rather prolonged fatigue

Pain commencing while the part is at rest is rarely the first symptom. This is a late symptom of advanced and severe disease Rest pain is always present if there is an acute arterial occlusion Night pain occurs in the toes, the foot and the lower part of the leg It is often a persistent aching, sufficient to interfere with sleep

Moderate to severe pain is associated with ulceration and gangrene Pretrophic pain, like rest pain, is usually worse at night than in the daytime. Pretrophic pain may be so severe that it is not controlled by the administration of opiates

When there is prolonged disuse of the joints, stiffness and even ankylosis may develop. At least a part of this joint stiffening is secondary to the muscular weakness characteristic of insufficiency of the peripheral circulation.

EXAMINATION On examination of a patient who has arteriosclerosis obliterans the findings are those of occlusive arterial disease. A decrease in the size of the pulsations in the peripheral arteries is present. The absence or impairment of pulsation in the dorsalis pedis artery is not necessarily significant Pulsations, though they may be very weak, are usually present in the posterior tibial, popliteal and femoral arteries when the patient is at rest in a warm environment.

The color of the feet is not changed until the arteriosclerosis obliterans is moderately advanced. When the disease is more severe, the toes of one or both feet or an entire foot are erythematous. Later the reddish color changes to a bluish discoloration or pallor. Immediately after an acute arterial occlusion the foot is pale and appears shrunken.

Postural color changes, such as pallor on elevation and a delay in a return of rubor on dependency, are pathognomonic of occlusive arterial disease. Some idea of the severity of the arterial insufficiency may be obtained as follows: If the feet are elevated for 2 minutes and then placed suddenly in the dependent position, failure of the color to return within 15 seconds indicates a moderate degree of

and nonvascular diseases. The vascular diseases to be differentiated are Raynaud's disease, acroscleroderma, livedo reticularis, acrocyanosis, erythermalgia or erythromelalgia, pernio, ergotism, acute thrombophlebitis of large veins, venous insufficiency and varicose veins.

The diseases which are not at least primarily vascular (nonvascular) which may require differentiation are frostbite, trophic ulcers and gangrene associated with organic disease of the nervous system, pronated feet, metatarsalgia and other mechanical derangements associated with the flatfoot syndrome.

The prognosis of thromboangiitis obliterans as to the loss of life or limb is difficult to estimate

Arteriovenous Fistula. The terms pulsating angioma, cirsoid aneurysm, arteriovenous aneurysm, varicose aneurysm, cavernous angioma, aneurysm by anastomosis, arteriovenous varix, aneurysma serpentina, angioma plexiforme, angioma arteriale, angioma arteriale serpentinum and angioma arteriale racemosum have been employed to designate or to indicate arteriovenous fistula.

Arteriovenous fistula most commonly is acquired, but it does occur as the result of congenital malformations

Congenital Arteriovenous Fistula. Congenital arteriovenous fistula results from failure of differentiation of the common embryologic anlage into artery and vein There is a persistence of the vessels or communications which are normal in the primary anlage.

Congenital arteriovenous fistulas occur anywhere in the body, for instance in the bones, cranium, middle ear and all of the parenchymatous organs. The only easily demonstrable congenital arteriovenous fistulas occur in the extremities.

SYMPTOMS OF ARTERIOVENOUS FISTULA IN THE EXTREMITIES. When varicose veins appear without obvious cause over a leg or an arm of a child, particularly when associated with ulceration or elongation of the limb, a congenital arteriovenous fistula is suspected. In some instances of congenital arteriovenous fistula the enlarged, varicose, tortuous veins may pulsate

Ulceration attributable to fistula may affect the hands, whereas chronic venous insufficiency attributable to ordinary varices or to thrombophlebitis is singularly absent from the hands

EXAMINATION Hemangiomas (birthmarks), cavernous or diffuse, port-wine color or bluish red, are present in somewhat more than half of those who have congenital arteriovenous fistula affecting the extremities. Associated with hemangiomas may be an increased growth of hair and increased sweating

Thrills and bruits are absent in congenital arteriovenous fistula Examination to establish the presence of an arteriovenous fistula includes analysis of the composition of the blood near the fistula Arterialization of the venous blood invariably occurs. For analysis the blood is withdrawn from a vein proximal to the fistula on the involved side and from a vein in a similar location on the normal side. The blood from the vein of the involved extremity has an oxygen saturation which varies from 5 to 45 per cent greater than that from the normal extremity.

Arteriography is performed after local anesthetization The contrast medium is ejected from the syringe into the occluded artery proximal to the site of suspected arteriovenous fistula A series of four or five arteriograms is made in rapid succession Demonstration of the opaque medium in the veins above the point of injection in the first arteriogram when the artery is closed by digital pressure is diagnostic of arteriovenous fistula The amount of filling of the venous trunks is proportional to the size of the fistula or fistulas Correct interpretation is made only by those experienced in the performance and in the interpretation of the results of arteriography.

DIAGNOSIS The diagnosis of arteriovenous fistulas of congenital origin depends on differences in oxygen saturation of the venous blood or on the results of arteri-

Allen, Barker and Hines separate cases of thromboangiitis obliterans into four groups on the basis of the clinical course: (1) In the *nonprogressive type, after one or two episodes of arterial occlusion further episodes fail to develop and a period of circulatory compensation follows which may last for many years. (2) A slowly progressive clinical course characterized by episodes of mild to moderate arterial occlusion which occur at long intervals apart Between episodes are quiescent periods of weeks to months, even years, when there is some improvement in the circulation as the result of development of arterial anastomoses. Finally the active lesions may cease to develop, and then the patient is left with a moderately to severely damaged arterial tree. (3) In some patients a sudden arterial occlusion of large vessels occurs and the result is extensive gangrene If gangrene does not supervene, convalescence is slow and severe arterial insufficiency persists. (4) Rapidly progressive or fulminating instances of the disease, with widespread gangrene necessitating amputation of the legs and perhaps some of the fingers, occur but are rare.

EXAMINATION The extremities may appear a normal color if the patient is in bed If the extremities are in a dependent position, they are often red or cyanotic

Asymmetric postural color changes frequently are found in thromboangiitis obliterans Raynaud's phenomenon may occur in association with thromboangiitis obliterans Affected parts become abnormally blanched after a short period of elevation, and on dependency after elevation there may be a delay of 5 to 60 seconds before the color returns to the skin and before the superficial veins again become visible. After the return of color the part usually becomes abnormally red

The pulsations in the posterior tibial and dorsalis pedis arteries are impaired or absent in the great majority of cases of thromboangiitis obliterans. Impairment or absence of radial or ulnar pulsations occurs in less than one half of those who have the disease. Impairment or absence of pulsations in the dorsalis pedis artery is present as the result of anomalies of the artery in 1 of every 10 normal persons Pulsations in posterior tibial arteries may be said never to be absent as a result of congenital anomalies

Ulceration and gangrene may occur spontaneously, but frequently they follow mechanical, chemical or thermal trauma The sources of trauma often precipitating gangrene are injury from nails in shoes, bruises, nicks or cuts in the skin from trimming nails and corns, or from other treatment of corns by freezing or burning, and the injudicious use of strong or irritating medicaments or chemicals Nail growth is slow The nails may be thickened or thinned and deformed The digits and sometimes an entire foot appear shrunken owing to the atrophy of the muscle and absorption of fat. The bones are osteoporotic on roentgenographic examination Gangrene of the hand or arm is rare.

Edema of the affected extremity or extremities is a common finding A red, cold, swollen foot with ulceration or gangrene of one or more toes is commonly seen in thromboangiitis obliterans Superficial thrombophlebitis in association with definite occlusive arterial disease is characteristic of thromboangiitis obliterans

DIAGNOSIS. A diagnosis of thromboangiitis obliterans is made when it is established that there is organic occlusion of peripheral arteries. In a young man the absence or marked impairment of peripheral arterial pulsations and the presence of asymmetric temperature and postural color changes of digits of the feet or hands are diagnostic. A dry gangrene of one or more digits which cannot be attributed to

livedo reticularis of the legs and (4) xanthoma tuberosum.

Thromboangiitis obliterans may have to be differentiated from a host of vascular

Raynaud's Disease and Phenomenon. Raynaud's syndrome occurs both as a primary disease entity and as a secondary result of a number of etiologic factors.

Primary Raynaud's Disease. The cause of the primary Raynaud phenomenon is not known The disease is peculiarly common in girls and women and usually begins about the onset of menstruation, although the first appearance may be as late as 35 to 40 years of age. It is frequently observed that more than one member of the family of the patient has suffered from cold hands or feet, "dead fingers" or other manifestations of vasospasm The importance of morbid heredity in this disease, however, has not been evaluated

Among the known contributing factors for precipitation of symptoms cold is important. The color changes are first observed after exposure to cold Emotional and nervous upsets, commonly bring on Raynaud's phenomenon, although not so commonly as cold.

The varying degrees of color changes in Raynaud's disease are related to transient changes in blood flow to the digits and are confined largely to the digital arterioles. The changes in the digital arterioles may result from either local faults or central vasomotor factors Local faults in the digital arterioles seem to be responsible when Raynaud's phenomenon is produced only by exposure to cold Central vasomotor faults seem to be responsible when the phenomenon occurs only after emotional upsets or nervous tension.

SYMPTOMS. The first symptom of Raynaud's disease comprises color changes of the skin over the tips of the fingers and occasionally over the toes on exposure to cold These color changes usually begin slowly, often being present in some degree for a period of years, but they may be called to the patient's attention by an acute episode of pallor in one or two fingers on exposure to cold As the disease advances, more fingers are affected, and the extent of the disease in each finger increases until the whole digit is involved, finally the backs of the hands may become affected. The color changes progress successively through pallor, cyanosis and rubor. Pallor is present while the finger is cold Cyanosis may be present with pallor, giving the lifeless hue so characteristic of the disease. Rubor comes on warming the hands. Pain is not a prominent symptom during the attack or in the interval between attacks.

Paresthesia, consisting of numbness, tingling, burning, a feeling of tightness, and a sensation of pins and needles or sticking in the fingers, may occur during the attack In some cases a slight swelling of the involved fingers may occur and even persist during the interval between the attacks.

In the advanced stages of Raynaud's disease the patient may become disabled from the attacks, which occur at any time on exposure to a cool environment or from any emotional stress After the disease has progressed thus far, the attacks may be as frequent and severe in warm weather as in cold weather

Extensive gangrene does not occur in Raynaud's disease, although gangrenous ulcerations may arise on the tips of the digits and cause considerable pain and discomfort In an occasional instance these lesions may become infected and require amputation of the distal parts of the involved finger or fingers

EXAMINATION In the interim between attacks in the mild forms of the disease no abnormalities will be observed on examination. To confirm the diagnosis, it may be necessary to induce the phenomenon by immersion of the extremity in cold water or by its exposure to cold air The extent, nature and duration of the color changes indicate the severity of the disease

Tests for postural color changes are conducted for detection of possible occlusive arterial disease Each peripheral artery is palpated, and if questionable pulsations are detected in an artery, help in making the decision may be gained by occlusion of the other artery or arteries to the region while palpation is continued in the questionable artery

When Raynaud's phenomenon occurs in an arm and is more marked *on one side* than on the other, a scalenus anticus syndrome is suspected as well as a cervical rib

ography. These methods may be used for the detection of arteriovenous fistulas occurring in any accessible regions of the body.

It is usually impossible to correct congenital arteriovenous fistula by surgical means.

Acquired Arteriovenous Fistula. Acquired arteriovenous fistula of the extremities almost invariably is caused by penetrating wounds. These communications may occur in any part of an extremity. The passage of the arterial blood directly to the venous blood indicates an arteriovenous fistula irrespective of how devious the means of communication may be.

SYMPTOMS. Trauma which causes an arteriovenous fistula is followed by profuse and easily controlled hemorrhage.

After trauma the occurrence of varicose veins, edema, stasis pigmentation, ulceration and chronic indurative cellulitis round the spot where the fistula is situated indicates that the stab wound has not healed in the usual manner. Ulceration and stasis ulcer in acquired arteriovenous fistula are characterized by cutaneous changes and other changes in the entire portion of the extremity distal to the fistula as contrasted with venous insufficiency from other causes in which the ulcerations are limited to the surfaces over the malleoli.

Gangrene of distal portions of the extremity may occur as the result produced by shunting the arterial blood away from the capillary bed in the affected parts.

If an arteriovenous fistula is acquired before the epiphyses close, there is an increased length of the affected extremity

EXAMINATION On examination a thrill and a bruit continuous throughout the cardiac cycle can be felt and heard They are accentuated during systole and are diminished during diastole

The temperature of the skin of the extremity affected is increased distal to the fistula This warmth of the skin is characteristic of arteriovenous fistula

A few patients who have traumatic arteriovenous fistula are found to have enlargement of the heart A small fistula causes little, if any, increase in the size of the heart; a fistula of moderate size produces moderate cardiac dilatation, a large fistula invariably produces marked cardiac dilatation and often congestive failure. When enlargement of the heart occurs in cases of arteriovenous fistula, the changes which seem directly responsible are (1) a great increase in cardiac filling owing to acceleration of the velocity of blood and (2) an increase of effective venous pressure of the involved vein and anatomically associated tributary veins proximal to the fistulous connection. The volume of the returning venous blood is increased because of enlargement of the artery and vein in the fistulous circuit

An increased amount of oxygen in the venous blood proximal to the fistula is indicative of arteriovenous fistula. When the fistula is closed by digital pressure, bradycardia (Branham's sign) is often present The systolic and diastolic blood pressures may increase simultaneously with the slowing of the heart rate Since the artery empties directly into the vein, the pressure within the vein approaches that within the artery. The veins may actually pulsate

The cardiac output may be increased or even doubled in the presence of a fistula of moderate size. The increased cardiac size is primarily an adjustment dilatation, and cardiac hypertrophy is responsible for only a small degree of the increase in the size of the heart.

It has been observed by Porter and Baker that an extreme degree of cardiac dilatation can exist over a long period without cardiac failure. If the fistula is large, congestive cardiac failure and death may ensue if the fistula is not repaired

DIAGNOSIS. The presence of a machinery-like thrill and bruit which are accentuated during systole and diminished during diastole is sufficient evidence to enable one to make the diagnosis of traumatic arteriovenous fistula.

The fistula should be closed surgically.

of acute onset result from an arterial occlusion or an acute, severe arteriospasm which is a temporary occlusion of a segment of an artery.

When there is a more gradual onset after injury or operation, the vasospastic changes begin weeks or even months after injury or operation. In the presence of chronic irritation and infection plus the disturbed circulation, bone injury follows. In these cases, however, the osteoporosis may be largely due to inactivity or failure of normal stimulation and of use of the bone.

The symptoms of posttraumatic Raynaud's phenomenon are tenderness, edema and pain, and cold, moist, slightly cyanotic skin with or without roentgenologic evidence of osteoporosis in the region of, or distal to, the injury. The diagnosis is based on the history of trauma or operation preceding the appearance of symptoms.

NEUROGENIC RAYNAUD'S PHENOMENON. The disturbances of the central nervous system which are commonly enumerated as being associated with functional disturbances of circulation are hemiplegia, monoplegia, chronic anterior poliomyelitis, peripheral neuritis, progressive muscular atrophy, myelodysplasia, syringomyelia, causalgia, spina bifida and cord tumors The vascular manifestations consist of persistent pallor and coldness with or without other color changes.

Usually the distinction between functional vascular disturbances secondary to neurogenic disorder and manifestations of organic vascular disease is not difficult. There are coldness and often color changes which are out of all proportion to the objective evidence of occlusive arterial disease.

INTOXICATION In ergot poisoning both vascular and nervous symptoms are observed The vascular manifestation is gangrene, that of poisoning of the central nervous system may be convulsions In some cases, however, both neurologic and vascular symptoms occur which produce a feeling of intense heat and cold, burning pains (St Anthony's fire) and coldness and cyanosis of the extremities. In the severe forms the cyanosis is replaced by gangrene which may appear suddenly. The neurologic symptoms consist of severe psychic disturbances, paresthesia, muscular spasms and convulsions, and in some cases residual anesthesia of the skin and even permanent contraction of the muscles and paralysis of the extremities may be present The neurologic manifestations are more likely to occur in persons who are malnourished than in those who are well nourished

Cases of Raynaud's phenomenon and severe vasospastic disturbance leading to gangrene from the ingestion of ergot preparations for medicinal purposes have been recorded However, large doses of ergot preparations are usually tolerated without any untoward vascular manifestations

Scleroderma. The terms acroscleroderma, acrosclerosis and diffuse scleroderma have been used as synonyms of scleroderma Allen, Barker and Hines accept the term acroscleroderma with Raynaud's phenomenon as designating a scleroderma of the extremities, face and thorax which develops as a late manifestation of Raynaud's disease They restrict the meaning of the term sclerodactylia to a scleroderma which is limited to the fingers Acroscleroderma, used alone, implies a sclerodermic involvement of the skin of the face, thorax and extremities without reference to Raynaud's phenomenon (see page 1357)

Livedo Reticularis. Livedo reticularis (also called livedo racemosa, livedo annularis and asphyxia reticularis) is similar in many respects to other vasospastic disorders The etiology is unknown

Since the condition is of a vasospastic nature, it causes narrowing of the arterioles with an accompanying dilatation of the capillaries and venules The complaint is a persistent bluish to bluish red mottling of the skin of the legs and feet which occasionally extends to the thighs In some instances the hands and arms and the lower part of the trunk are affected The livedo never entirely disappears spontaneously. It is more noticeable on exposure to cold than under other circumstances.

Some patients have coldness, numbness, dull aching and paresthesia of the feet and legs. A few have chronic ulcerations of the skin of the legs. Occlusion of the

or pressure from the scalenus anticus muscle. Sclerodermatous changes may be associated with Raynaud's disease, or the disease may be secondary to generalized scleroderma.

DIAGNOSIS In the majority of instances Raynaud's disease can be diagnosed if there can be elicited a history of episodes of bilateral Raynaud's phenomenon precipitated by cold or emotion On examination there is an absence of primary disease, such as occlusive arterial disease, cervical rib or organic disease of the nervous system which could cause the phenomenon.

When Raynaud's phenomenon has been restricted to one finger or to one extremity for a long time, some secondary causative factor should be suspected When Raynaud's phenomenon occurs in a man, it should be suspected as being due to thromboangiitis obliterans or to some other factor until conclusively proved to be otherwise. If on examination gangrene which results from Raynaud's disease is present, it will be limited to the skin. Sclerodermatous changes and ulceration may complicate Raynaud's disease, but these are strictly limited to the skin and no involvement of any visceral organs will be found

Patients who have Raynaud's disease are treated medically or surgically. In selecting patients for surgical treatment, only those who have trophic changes and scleroderma should be considered Surgical intervention may decrease their disability in cold weather

Secondary Raynaud's Phenomenon. The term secondary Raynaud's phenomenon is employed to designate local changes in the peripheral circulation which permit of changes in color of the skin resembling those of the primary disease. Allen, Barker and Hines have classified the conditions or diseases in which secondary Raynaud's phenomenon may be observed as follows: (1) after trauma: related to occupation and following injury or surgical operation, (2) neurogenic lesions: cervical rib and scalenus anticus syndrome and diseases of nervous system; (3) occlusive arterial disease arteriosclerosis obliterans, thromboangiitis obliterans and embolism; (4) intoxication, for instance from heavy metals and ergot; (5) miscellaneous diseases such as scleroderma, lupus erythematosus and paroxysmal hemoglobinuria.

POSTTRAUMATIC RAYNAUD'S PHENOMENON. Two types of posttraumatic Raynaud's phenomenon may be observed (1) occupational Raynaud's phenomenon and (2) persistent vasospasm or Raynaud's phenomenon following injury or surgical operation

Occupational Raynaud's Phenomenon This is well illustrated by pneumatic hammer disease The rapid oscillations of the pneumatic hammer seem to sensitize the digital vessels of some workmen so that Raynaud's phenomenon occurs readily on exposure to cold There is a wide range of susceptibility to this injury Some workmen are not injured, even after very long periods of using the air hammer

The episodes of Raynaud's phenomenon usually appear first in right-handed men in the third, fourth and fifth fingers The phenomenon does not occur during work unless the tool is cold when in use In susceptible persons the attacks begin within two months to a year after the worker has started to use the hammer. The course of this condition is benign Often workmen are not greatly concerned about the vasospastic phenomena, but accept them as being a part of their occupation

Raynaud's phenomenon may be present in pianists and typists. The vasospastic discomforts involve only one or two digits Once the phenomenon is present, it will continue to be precipitated by exposure to cold even if there has been a change in the occupation.

Following Injury or Surgical Procedure Raynaud's phenomenon may come suddenly, soon after trauma or operation, or may be delayed for weeks or months The phenomenon may be associated with an osteoporosis (Sudeck's atrophy). Instances

SYMPTOMS. The symptoms of obstruction of the superior vena cava are often a throbbing sensation, headache, vertigo and sometimes mental confusion These symptoms are exaggerated by stooping, bending forward or physical exertion. They are likewise increased in the recumbent position, relief is often obtained while the patient is in the sitting or in the half-reclining position. A rapidly developing obstructive lesion produces congestion and an intense edema of the face, shoulders and arms.

EXAMINATION. Cyanosis of the face and upper extremities, and prominence, engorgement and dilatation of the veins of the head, neck, arms and upper part of the thorax are often present

The site of obstruction in the intrathoracic veins and the veins of the upper extremities and head can be determined accurately by determining the limitations of the evidence of increased venous pressure, edema and congestion If the veins of the neck and both arms are involved, the obstruction is situated in the superior vena cava. If a prominent plexus of large veins is seen over the sternum connecting with branches of the internal mammary vein, the obstruction is probably above the level of the azygos vein If the entire superior vena caval system is obstructed, large collateral veins are noted crossing the costal margin, and the blood flows downward over the anterior abdominal wall.

The direction of flow of blood in a dilated superficial vein is determined by stripping out the blood of a vein and compressing both ends of a segment thus freed of blood with the fingers, repeat this procedure and each time remove alternately the two fingers. When the finger in the direction of the blood flow is removed, the vein fills slowly if at all, whereas when the finger opposing the flow is removed, the vein fills rapidly

DIAGNOSIS. Roentgenographic examination, bronchoscopic examination and, if there are enlarged cervical lymph nodes, biopsy of the lymph nodes in the neck or axilla are each of diagnostic value The tumors which produce obstruction of the superior vena cava are nearly always malignant.

Obstruction of the Inferior Vena Cava. Obstruction of the inferior vena cava usually results from thrombosis or thrombophlebitis However, neoplasms, aneurysms, ascites and constriction as the result of adhesive bands and scar tissue from old inflammatory processes and accidental surgical ligation cause inferior caval obstruction

Pain may be present and severe soon after the obstruction It soon subsides. There are bilateral enlargement of the lower extremities with edema, extensive prominence of the superficial veins of the legs, and the presence of dilated and often tortuous superficial veins on the abdomen which extend well up to the thorax. The direction of blood flow in these collateral veins is upward

Edema of the lumbosacral region is frequent Bilateral obstruction of the common iliac veins without obstruction of the inferior vena cava can produce similar findings The occlusion of the inferior vena cava may extend above the level of the renal veins and thus may be incompatible with life. Instances of ligation of the inferior vena cava have occurred without an ensuing edema of the legs or dilated veins

Nonobstructive Diseases of Veins. ***Phlebosclerosis.*** Degenerative lesions of the veins are exceedingly rare. Occasionally there occurs calcification of the medial coat. However, the so-called calcified lesions of the veins which are seen in roentgenograms of the extremities and of the pelvis are calcified thrombi (phleboliths)

Phlebosclerosis, or venofibrosis according to Allen, Barker and Hines, occurs between the ages of 18 and 45 years. The etiology of the condition has been ascribed to gout, lead poisoning and syphilis, and perhaps in some way it may be associated with peptic ulcer

arteries of the toes and gangrene have developed in a few who have this disease.

On inspection of the extremities the reticular, blotchy nature of the color changes is characteristic. The diagnosis can be readily made from the appearance of the extremities. Rarely does this disease cause any serious consequences, though once established it is always present. The disease is common in women who have fat legs

Acrocyanosis. Acrocyanosis seems to represent a generally unstable vasomotor system Lewis and Landis concluded that the fault is local. The disease is often a familial one which is suggestive of morbid heredity. The cause of the disease is unknown.

The disease affects women. They complain of constant coldness and bluish discoloration of the fingers and hands which is worse during the winter than at other seasons.

Examination of the peripheral arteries will not reveal any evidence of occlusive arterial disease. The color changes of acrocyanosis are persistent as contrasted with the intermittent nature of the color changes in Raynaud's disease. There is no history of episodes of blanching, and no scleroderma or development of trophic changes, ulceration and gangrene

DISEASES OF THE VEINS AND LOCOMOTION

Veins of the Leg and Foot The veins of the lower extremity are divided into superficial and deep. The deep veins all have valves and there are frequent communications with the superficial veins.

On the dorsum of the foot is a venous arch which unites with the medial dorsal digital vein to form the commencement of the long saphenous vein

The external or short saphenous vein begins behind the external malleolus, ascends alongside the Achilles tendon, thence over the gastrocnemius to empty into the popliteal vein. Its branches anastomose with those of the long saphenous on the inner side of the leg, and it communicates through the deep fascia with the deep veins It is accompanied by the external saphenous nerve

Obstructive Diseases of Veins. Venous obstruction arises from extrinsic and intrinsic causes. The possible extrinsic causes are numerous; the commonest is a partial obstruction of the *iliac veins* by a gravid uterus during the last months of pregnancy. Varying degrees of venous insufficiency of the limbs as well as permanent damage to the veins of the lower extremities and their valves may result from gestation

Another common cause of venous obstruction of the iliac veins is pressure from pelvic and abdominal neoplasms. Neoplastic obstruction (lymphoblastomas and metastatic carcinomas) is a common cause of obstruction of the iliac veins and also of the superior and the inferior vena cava

The intrinsic cause of obstructive disease of the veins is mainly thrombophlebitis which will be considered later

SYMPTOMS. The signs and symptoms of extrinsic obstruction of the iliac veins as well as the veins distal to them are enlargement of the extremity or extremities distal to the obstruction, with or without edema, congestion of the skin, prominence of the superficial veins, sometimes dilatation to the point of formation of a varix, and increase of venous pressure. Pain is not severe. Some pain from a congestive distention in muscles of the extremity or extremities may occur on dependency. This discomfort is relieved by elevation of the affected member.

EXAMINATION. In many instances the cause of the obstruction of the iliac veins is easily determined by examination by physical means of the pelvis and the rectum

Obstruction of the Superior Vena Cava. Obstruction of the superior vena cava is a rare condition The causes of obstruction of this vessel are mediastinal tumors, chronic mediastinitis, thrombophlebitis, constrictive pericarditis and congestive heart failure.

Pain, swelling and tenderness vary with the severity of the inflammation and the degree of congestion distal to the site of obstruction Fever, tachycardia and malaise are variable among patients who apparently have the same degree of local involvement. Thrombi in superficial veins are palpable.

Thrombophlebitis of the saphenous systems is often secondary to infectious disease, cachectic states, or blood dyscrasias The multiple lesions appear as red, painful, tender, raised linear ridges in the skin In small superficial veins the lesions may be palpated as firm, cordlike segments in the course of a visible vein. The inflammatory reaction undergoes involution in from 7 to 18 days but the thrombosed portion of the vein can be felt for a much longer period In some instances, in the presence of arterial insufficiency, necrosis of the skin occurs over the lesion (necrotizing phlebitis).

The muscular veins and deep veins of the calf are commonly affected by postoperative thrombophlebitis. When this occurs, there are pain in the calf and tenderness in the calf muscles Dorsiflexion of the foot will occasionally cause pain in the calf in some early and otherwise subclinical thrombosis of the muscular or deep vein of the calf (Homans' sign) The presence of pain and tenderness in the calf during the immediate postoperative period may denote a thrombophlebitis of the short saphenous, muscular or deep tibial veins

Thrombophlebitis of the popliteal and the femoral veins causes pain and some transient swelling and congestion of the lower part of the leg and the foot There may or may not be fever Iliofemoral thrombophlebitis is characterized by a fairly sudden onset of fever and pain present along the course of the affected vein and thence passing distalward to the foot The pain may begin in the gluteal region or in the calf The superficial veins are somewhat prominent and distended, and the skin may be diffusely or locally cyanotic There is enlargement of the entire extremity.

Pain and often local swelling and redness at the site of the thrombosis followed by enlargement of the extremity and often fever are *diagnostic* of thrombophlebitis A superficial thrombophlebitis involving small veins is distinguishable by the linear rather than circular shape of the lesions, their smaller size, lack of ulceration and comparatively rapid involution Deep thrombophlebitis of the calf may resemble myositis, fibrositis and sciatic pain except that there is prominence of superficial veins

COMPLICATIONS AND SEQUELAE Chronic venous insufficiency of the limb is a serious complication of iliofemoral thrombophlebitis and saphenous thrombophlebitis

Phlebothrombosis (*Secondary Thrombophlebitis, Marantic Thrombophlebitis*). In phlebothrombosis there is no evidence of antecedent disease or injury of the vein Thrombosis is first The phlebitis develops as a reaction to the thrombosis

[illegible]

infectious trauma to pelvic veins may form a locus for the development of an extending thrombus in some cases However, after delivery multiple thrombi occur in small veins and venules of the uterus, there are changes which occur abruptly in the large dilated veins in the region of the broad ligaments, there is the loss of blood during delivery, and there are subsequent changes in the constituents of the blood itself.

Embolism, usually in the lungs, is the most serious complication of postoperative venous thrombosis It is the result of phlebothrombosis and occurs in many cases in which there is no clinical evidence of thrombophlebitis. Therefore it is assumed that thrombosis has occurred in some one of the peripheral veins and that either the entire thrombus became the embolus, or the part of it which remained at the original site failed to produce local symptoms.

The veins are small. A loss of endothelium and a hyalinization of the denuded surface are followed by subintimal fibrosis

Venofibrosis rarely produces clinical symptoms.

On palpation there is the sensation of hard cords which are small, mobile and smooth. Frequently a longitudinal groove in the skin corresponds to the location of the involved vein. The diagnosis is made on the forementioned findings.

Rupture. A vein rarely ruptures spontaneously unless diseased. Rupture is usually caused by trauma The rupture of a vein is rarely of serious importance so long as the skin is intact. The hemorrhage from a ruptured vein is limited by the tissue pressure and the formation of a hematoma.

Thrombophlebitis, Phlebothrombosis and Pulmonary Embolism. Thrombophlebitis is phlebitis in which a thrombus is present. By some it is defined as partial or complete venous occlusion by an intravascular thrombus which is associated with inflammation of the wall of the vein and has a firm mural attachment Phlebothrombosis is an occlusion of a vein by an intravascular thrombus which is not associated with inflammation of the wall of the vessel, is loosely attached to the wall and so can be easily detached, resulting in pulmonary embolism.

Thrombophlebitis. Thrombophlebitis occurs (1) as a local thrombophlebitis, (2) as suppurative thrombophlebitis, (3) as spontaneous thrombophlebitis, (4) as ischemic thrombophlebitis, and (5) as nonrecurring idiopathic thrombophlebitis

In *local thrombophlebitis* there is direct injury or a pre-existing disease of the wall of the vein The common example of this condition is the thrombophlebitis produced as a result of an injection of a sclerosing solution

Thrombophlebitis may originate at the site of contusions, lacerations and fractures even though there is no evidence of infection of the tissues.

A large number of lesions, usually of the smaller veins or venules, which occur as a part of inflammatory but nonsuppurative lesions are classed as thrombophlebitis of inflammatory or toxic origin These thrombi may be minimal or moderate in extent but are rarely extensive Examples of these lesions are the venous occlusions which occur in association with erythema nodosum, tuberculosis, gummas and granulomas

Suppurative thrombophlebitis may occur as the result of involvement of the wall of the vein by a severe suppurative disease. In these cases the thrombus itself is highly infected

Spontaneous thrombophlebitis may occur in varicose veins A history of minor injuries to a varix or constriction by a tight bandage or garter may be elicited In some cases thrombophlebitis may develop in varicose veins after operations, childbirth or infectious disease.

In extremities in which there is arterial occlusion with the consequent *ischemia* an extensive *secondary thrombosis* of the veins is often observed The venous occlusion is usually of little importance in comparison with the arterial disease.

Thrombophlebitis may develop primarily without any known injury to the vein in cases in which operation has not been performed, delivery has not occurred, and there has been no evidence of infectious disease, noninfectious systemic disease, or blood dyscrasia.

Patients who have gout or those who have gouty inheritance may have thrombophlebitis migrans, in which the lesions are usually bilateral and appear to migrate or jump from one vein to another.

Idiopathic thrombophlebitis of the nonrecurring type often involves a large vein in a lower extremity of a patient otherwise healthy It has the same clinical features as secondary or complicating thrombophlebitis No significant predisposing factors with regard to age or sex are known (Allen, Barker and Hines).

In all types of thrombophlebitis there is objective evidence of thrombosis and inflammatory reaction in the various coats of the venous wall at the site of the formation of the thrombus. The red or coagulation thrombus, the white or agglutination thrombus, and the mixed thrombus are described The commonest type of thrombus is the mixed type

the internal malleolus, or occasionally on the feet or toes if the patient has gone barefooted. These ulcers often become chronically infected and odorous.

Perthes' test for occlusion of the deep veins of the legs is based on the physiologic actions of the skeletal muscles in the leg which influence the venous circulation toward the heart. During contraction of the muscles in the leg in walking there is a compression to the deep veins, resulting in a constriction and forcing the blood to pass upward toward the heart During muscular relaxation the empty and collapsed deep veins fill again with blood aspirated from the superficial veins. This is known as the diastolic phase or muscular diastole.

The Perthes test consists in placing a tourniquet around the thigh just above the knee, constricting the superficial long saphenous vein sufficiently to prevent the reflux of venous blood, and having the patient walk vigorously or flex and extend the knee repeatedly. The interpretation of this test is as follows:

1. *If the varicosities in the leg collapse during muscular contraction, the deep vein* is patent, permitting the blood to pass into the deep circulation through the deep communicating veins and up toward the heart. This is known as a Perthes negative and permits treatment to the varicosities.

2. If the varicosities do not collapse but become more distended and the patient feels pain or severe cramps in the leg during muscular contraction, the blood cannot pass through the deep circulation and up to the heart because there is an occlusion or thrombosis in the deep vein—positive reaction.

In the presence of certain segmental thromboses or segmental occlusions in the deep vein in the thigh the usual Perthes reaction may be erroneously negative. Barone has suggested carrying out Perthes' test at different levels of the leg to prevent such an error.

The modified test (Barone) is carried out as follows The tourniquet is placed first below the knee above the varicosities and the patient is instructed to walk as in the Perthes test If the veins below the tourniquet collapse, one repeats the test by placing the tourniquet 5 inches (about 13 cm) higher If the veins likewise collapse, one repeats the test again and again, each time placing the tourniquet at levels 5 inches higher up to the groin The interpretation is as follows (1) If the varicosities below the tourniquet collapse every time the patient walks with the tourniquet at different levels, for example

of an existing thrombus in the deep vein.

Diagnosis Chronic venous insufficiency is diagnosed (1) by edema of the legs which disappears after recumbency, (2) by dilatation and prominence of superficial veins, and (3) by a tendency to aching distress in the limb when the patient is in the erect posture, relieved by recumbency in a comparatively short time, particularly if the limb is elevated.

The leg ulcers are differentiated from syphilitic ulcers, which occur in the upper portion and often on the lateral aspects of the leg These ulcers are usually without the chronic induration and skin color changes of the varicose ulcer.

DISEASES OF THE LYMPH VESSELS AND LOCOMOTION

Lymphedema. Lymphedema is the manifestation of an obstruction to the central flow of lymph and the inability of the newly formed collateral channels to develop adequate valves As a result of stagnation of the lymph its protein content is increased, fibroblasts proliferate and the resultant fibrosis increases the stasis Thus as the stasis of lymph increases, the tissues are less viable and often inflammation is present, and then more stasis ensues

There are acute and chronic lymphedemas. The acute lymphedemas are commonly present during the course of acute infections

Chronic Lymphedema. Homans classified the chronic lymphedemas as primary and secondary.

Varicose Veins (Phlebectasia, Venous Aneurysm). Some varicose veins develop spontaneously, while others develop distal to a venous obstruction.

Varicose veins which develop spontaneously are the result of a hereditary weakness in the structure of the vein and its valves. The veins are constitutionally poor and are unable to withstand the normal amount of stress and strain resulting from increased abdominal pressure and abdominal obesity, or the opposite, emaciation, both of which are common as age increases. Atrophic lesions of the skin, such as diffuse idiopathic atrophy or acrodermatitis chronica atrophicans and extensive scars, occur

Varicose veins which develop distal to a venous obstruction are a late complication of obstruction of the vena cava.

Varicose veins affect both men and women

The essential demonstrable pathologic changes in varicose veins are (1) dilatation, (2) elongation and tortuosity, (3) loss of elasticity, (4) variations in the thickness of the wall and (5) disappearance of the valves of the veins.

SYMPTOMS. Often extensive varicose veins of the legs may not produce any subjective symptoms. When symptoms are present, they consist of an increased tendency to fatigue of the leg muscles, a sensation of fullness and congestion, and soreness in the region of the veins.

Superficially in the skin there may be an eczematoid dermatitis, pigmentation, paresthesias of burning, pain and itching in the region of varicose veins.

EXAMINATION Have the patient stand in good light with bare legs In most instances varicose veins are apparent on inspection In obese persons some varices, particularly of the long saphenous vein and of other veins, can be detected and examined more easily by palpation, particularly with regard to their size and tortuosity.

The deep veins are almost always competent unless the patient has had iliofemoral thrombophlebitis previously. Iliofemoral thrombophlebitis frequently leaves the iliofemoral vein partially obstructed or with incompetent valves However, in these cases compression of the superficial veins by an elastic bandage is usually well tolerated by the patient.

Chronic Venous Insufficiency. Chronic venous insufficiency sometimes is called venous stasis, stasis edema, stasis eczema, stasis ulcer, varicose ulcer, or postphlebitic ulcer. The basic cause for chronic venous insufficiency is the destruction and deformity of the small venules and capillaries to the extent that insufficient numbers are left intact to carry on without abnormal congestion

SYMPTOMS The first and often the only symptom of chronic venous insufficiency is subcutaneous edema which occurs after standing and walking The edema is above the shoe tops It will develop in the feet if the patient wears loose shoes or slippers or no shoes or slippers at all The discomfort in chronic venous insufficiency is not great. A dull ache sometimes follows prolonged standing, but will go within five to thirty minutes when the leg is elevated If a patient who has osteoarthritis of the knees has venous insufficiency, the joint changes are often more severe. In the presence of ulcers and indurative cellulitis the pain is more intense.

EXAMINATION. There may or may not be cyanosis of the skin. The skin over the edematous regions may be irregularly covered by areas of brown pigmentation (hemosiderin) Associated with the pigmentation often there is dermatitis or eczema. The eczema frequently is of a chronic scaling variety accompanied by minimal subjective manifestations. It may be limited to the medial aspect over the lower third of the tibia. A more diffuse eczema may be present.

A hard, brawny induration of the skin and subcutaneous tissues may be present If the skin is depressed over the entire circumference of the ankle and lower part of the leg, or just in spots, an indurated cellulitis is present. Ulceration may be present and if so, this is one of the common and disabling manifestations of chronic venous insufficiency. These ulcerations appear just below the malleoli, especially

Advanced lymphedema offers no diagnostic difficulties. The brawny, indurated skin and hypertrophied limb of advanced lymphedema bear little resemblance to manifestations of edema in other diseases It is only when lymphedema is not associated with changes in the appearance and texture of the skin secondary to inflammation that difficulty arises.

TUMORS OF BLOOD AND LYMPH VESSELS

Benign Tumors of the Blood Vessels. ***Telangiectasia.*** The commonest cause of telangiectasia is exposure of the skin, particularly of the face, to wind and sun A less common but well-known cause is excessive exposure of any part of the body to radium or roentgen rays. Telangiectasia is often associated with acne rosacea, xeroderma pigmentosum, lupus erythematosus, morphea and syphilis.

Four types of localized telangiectasia are described, namely, spider nevus, senile ectasia, hereditary hemorrhagic telangiectasia and pulsating telangiectasia.

A *spider nevus* (nevus araneus) appears as a raised red dot from which fine vessels radiate. The lesions occur on the face, neck, thorax, backs of the hands or other parts of the body. These nevi develop spontaneously during adult life and in those who have delicate skins However, they are of little clinical importance and treatment is not necessary

Senile ectasia, senile vascular nevus, appears as multiple small papillary lesions of a bright red or purplish color This vascular nevus does not imply the presence of any known visceral disease

Hereditary and familial hemorrhagic telangiectasia (Rendu-Osler-Weber syndrome) is characterized by the development of multiple telangiectatic lesions of the skin and mucous membranes The lesions occurring in the mucous membrane of the nose have a definite tendency to hemorrhage and cause frequent and often serious epistaxis by such minor trauma as sneezing, coughing, vomiting, or strain while lifting a heavy weight The presence of these lesions on the mucosa of the oral cavity, lips, tongue, pharynx or on the skin of the face and fingers may be the focus of excessive bleeding

[illegible] from the history of bleeding from a region where telangiectasia [illegible] originating from [illegible] The lesions may [illegible] tendency to blanch on pressure from a glass slide.

Pulsating telangiectasia (*pulsating hemangioma*) occurs on the face, hands and thorax of adults The lesions are larger (2 to 5 mm in diameter) and more raised than the lesions of hereditary hemorrhagic telangiectasia

The radiating, pulsating telangiectatic vessels are larger than those of spider nevi. The pulsations, if not obvious, can be demonstrated by making light pressure by means of a glass slide over the lesion

Pulsating telangiectasia occurs in association with hepatic disease, pregnancy and lymphosarcoma Severe hepatic disease was present in all of the cases reported by Williams and Snell These authors stated that telangiectasia preceded the development of the clinical signs and symptoms of hepatic disease. This does not mean, however, that all those who have severe hepatic disease have pulsating telangiectasia or that pulsating telangiectasia is always indicative of hepatic disease

Hemangioma. A hemangioma is a slowly growing, benign tumor composed of newly formed blood vessels. Hemangiomas are of congenital origin and are commoner in women than in men Occasionally the tumors increase in size with the onset of menses or during pregnancy

Hemangiomas are variously classified as nevus flammeus, capillary, cavernous, diffuse, racemose, cirsoid and congenital arteriovenous fistulas Several of these different kinds of hemangiomas may occur in the same individual

The *primary* lymphedemas comprise the hereditary or familial, the congenital, the praecox and, finally, the simple forms. The primary lymphedemas are noninflammatory and are somewhat commoner than the secondary noninflammatory lymphedemas.

PRIMARY LYMPHEDEMA (Lymphedema Praecox). The onset in the majority of cases is in adolescent girls. *There is an accentuation during menstruation* It has been postulated that the additional load thrown on the lymph vessels by rapidly developing reproductive structures induces functional incompetence or allows entrance of infection into the lymph trunks and nodes in the pelvis

Spontaneously and without any known cause the patient notices a puffiness about the foot or ankle, where in most instances it stops However, edema may progress up the leg, and often the entire limb may be involved within a few days or weeks. As *the condition develops, a smooth skin becomes roughened, the soft edema* becomes resistant to pressure, tissue hypertrophy occurs and the leg becomes permanently enlarged, unsightly, ungainly, uncomfortable, and disliked by the patient. A dull, heavy sensation is present Ulceration of the skin does not occur

HEREDITARY CONGENITAL LYMPHEDEMA (Milroy's Disease). This condition affects a sufficient number of blood relatives to indicate that a disturbance in the genes is responsible Its manifestations are the same as those of lymphedema praecox.

The pathologic changes in congenital lymphedema are characterized by thickening and canalization of the subcutaneous tissue and the adipose tissue. However, in this form of lymphedema there is neither thrombosis of lymph vessels or blood vessels nor evidence of inflammation. In other forms the foregoing changes are repeated, and in addition there is atrophy of muscle, nerve fibers and sweat glands, and evidence of infection by leukocytic infiltration.

The characteristics of congenital lymphedema are the presence at birth of a diffuse *swelling involving part or all of a single extremity; the disproportionate* increase in the size of the involved extremity as contrasted with the uninvolved companion member, the absence of pain, ulcers and recurrent attacks of infection, and the otherwise good health of the person affected.

The presence of a firm swellin [illegible] definitely reduced in size when the extremity is eleva [illegible] the enlargement is nodular rather [illegible] a single part. Congenital arteriovenous fistulas increase the length and the girth of the extremity The temperature of the skin is higher than that of the companion member. The superficial veins are dilated, and the oxygen content of the blood from superficial veins in the affected regions resembles that of arterial blood Congenital hypertrophy or congenital hemihypertrophy of an extremity is *rare and this condi*tion is rarely limited to a single member

SECONDARY LYMPHEDEMAS. Secondary noninflammatory lymphedema includes instances of occlusion of the lymphatics as the result of malignant tumors, surgical removal of lymph nodes, pressure, and irradiation therapy. Whether lymphedema that ensues on irradiation therapy is brought about by fibrosis caused by irradiation or by metastasis of the malignant disease for which irradiation is given cannot be *determined* with certainty

Inflammatory Lymphedema. Inflammatory lymphedema may be primary or secondary It may be a part or a result of venous insufficiency, trichophytosis, systemic disease or filariasis, or may be due to local tissue injury or inflammation.

All examples of inflammatory lymphedema, *exclusive of the chronic form,* have one feature in common; namely, single or recurrent attacks of acute cellulitis and lymphangitis

Pregnancy and systemic disease such as influenza, typhoid fever, pneumonia, malaria and filariasis may lead to recurrent attacks of cellulitis and *lymphangitis* and result in lymphedema.

anastomosis. This is an end-organ situated in the derma and cutaneous tissue and often beneath the nails. The conglomeration of tissue acts as a control of the peripheral circulation.

The glomus is compared to a thermostat in that anything which disturbs it should cause some disturbance of the heat regulation of the body. When a tumor develops in a glomus, the normal function is disturbed. When the lesion is touched or irritated by heat or, more often, by cold, the circulation of an entire half of the body may be disturbed by the vasomotor activation. A glomus tumor may occur at any age. Trauma is often associated with but probably is not the cause of glomus tumors.

SYMPTOMS. Pain may be present for a long time before the tumor becomes visible. These lesions are usually single although multiple tumors are recorded. Glomus tumors are not malignant.

EXAMINATION A glomus tumor is a small, purplish nodule either in the skin of an extremity or under the nail The tumor rarely exceeds a few millimeters in diameter.

These tumors are so exquisitely painful that touching the lesion usually provokes a paroxysm of severe pain A satisfactory method for examination for a glomus is to ask the patient to indicate with the tip of his finger the site of maximal pain. The adjoining skin is examined with the point of an ordinary steel pin. The normal or surrounding skin or nail, if the lesion is subungual, is not unduly sensitive, but the instant that slight pressure is made over the site of the glomus tumor the patient will withdraw the extremity from the hands of the examiner.

Anteroposterior and lateral roentgenograms of the digit may reveal a small excavation of the phalanx from erosion caused by the tumor.

DIAGNOSIS. The diagnosis is established by histologic examination of the glomus tissue.

The presence of a bluish or purplish lesion in the skin of an extremity, and especially under the nail of a digit which when touched causes the patient acute pain, is sufficient evidence to warrant suspicion of a glomus tumor. The exposure of the lesion to cold will produce neuralgia-like pain which seems to originate in the lesion and may spread to involve the entire extremity, and may produce vasomotor changes

The tumor should be surgically removed

Malignant Tumors of the Blood Vessels. ***Hemangio-Endothelioma.*** Hemangio-endotheliomas are malignant tumors arising from the endothelial cells of the blood vessels Hemangiosarcomas contain both fibroblastic connective tissue and vascular tissues.

Hemangio-endotheliomas occur in any part of the skin and subcutaneous tissue They begin as small tumors of millimeter size and increase to about 4 inches (10 cm) or more in diameter These tumors are dark red, whether situated in the skin or in the mucous membranes They are soft and have a tendency to ulceration and bleeding A hemangio-endothelioma situated in the gastrointestinal tract often causes exsanguinating hemorrhages A differentiation of benign hemangiomas and hemangio-endotheliomas is possible only by histologic study.

One type of hemangio-endothelioma (Ewing's tumor) involves the shaft of long bones, particularly the shaft of the femur Two thirds of Meyerding's patients who had this tumor were boys or men less than 30 years of age. The discomfort suffered by these patients was pain at the site of the lesion The correct diagnosis of these tumors can be made only by biopsy

Hemangio-endotheliomas grow slowly and metastasize slowly but there are many exceptions. When metastasis has occurred, the prognosis is grave.

The treatment of hemangio-endotheliomas without metastasis consists of wide surgical excision

Nevus flammeus (port-wine stain, birthmark) is a form of capillary hemangioma It is a flat well-demarcated purplish red discoloration of the skin which blanches easily on pressure Elevated small nodular tumors may be scattered through the lesion. The lesions vary greatly in size and may be multiple. They are commonest on the face, less common on the trunk or extremities. One of each 3 infants is born with a small nevus flammeus in the occipital region Most of these nevi gradually disappear as the children grow older. Occasionally a nevus of this type is disfiguring and extends over large portions or half of the body. Such an extensive lesion is usually present at birth. It does not extend but enlarges as the part grows. When nevus flammeus occurs on the lower extremities, it may be a part of deep-seated *cavernous hemangiomas or multiple arteriovenous fistulas.*

Capillary hemangiomas (strawberry nevi, capillary nevi) are circumscribed, finely lobulated, elevated, bright red to purple-red tumors which are present on the skin of the face or elsewhere at the time of birth. These tumors occur singly or multiply and vary from a few millimeters to several centimeters in diameter and may attain a thickness of 1 to 2 cm. They blanch incompletely on pressure.

Cavernous hemangiomas (nevi cavernosi, cavernomas) are tumors composed of masses of dilated thin-walled vessels and are the commonest type of true hemangiomas They are present at birth They often continue to enlarge throughout life Cavernous hemangiomas are multiple and occur in all organs of the body. The common situations are the face, neck, oral mucosa, extremities, liver, bones (par*ticularly the vertebrae), stomach and intestine. In a vertebra they have to be dif*ferentiated from Paget's disease and metastatic malignant lesions. On an extremity a cavernous hemangioma often involves skin, subcutaneous tissue and muscle It is a localized but poorly demarcated spongy tumor with multiple bluish, soft nodules resembling dilated veins just under the skin; on elevation of the part the tumor shrinks but usually does not disappear. Varicose veins may be associated

Diffuse hemangiomas (diffuse systemic hemangiomas) when present may involve a large part or all of one or more extremities, one side of the body or a large area over a shoulder and side of the thorax.

The extremity is usually enlarged and irregular. The lesions resemble varicose veins of varying sizes but look queer because they are all over the extremity. The *affected leg feels heavy and aches after walking. The lesions* tend to collapse on elevation Multiple arteriovenous fistulas may coexist but their presence is difficult to prove. Nevus flammeus may be associated.

The presence of phleboliths may be demonstrated by roentgenograms of the extremity.

Cirsoid hemangioma, sometimes designated racemose hemangioma, and known also as cirsoid aneurysm and congenital arteriovenous fistula, is a progressive and bone-eroding, pulsating lesion in the region of the neck which is similar to an extensive congenital arteriovenous fistula Cavernous hemangiomas and port-wine stains may be associated with multiple arteriovenous fistulas

Spontaneous involution often occurs in these angiomas; therefore it is well to wait *for several years before considering treatment. At the* very best, treatment of these conditions by the plastic surgeon is not all that is to be desired

For the treatment of cavernous hemangiomas and the mixed capillary and cavernous types about the face and neck Figi stated that the implantation of two to eight 0 5 millicurie radium seeds is the preferable treatment for young children

Glomangioma or Glomus Tumor. A glomus is a small conglomeration of blood vessels In the body there are various glomera, for instance, glomus caroticum, glomus carotideum, glomus choroideum and glomus coccygeum. Tumors may arise in any of these glomera, but here interest is on the cutaneous glomus, digital glomus or the neuromyo-arterial glomus, which is the total unit making up a Sucquet-Hoyer

axilla, groin, retroperitoneal space, pelvis, thoracic wall or sacral region. The cystic mass is compressible and thin-walled and transilluminates well Cystic hygromas become infected after respiratory infections, surgical operation or radiation, and when such infections occur, they are always serious and may be fatal. If treatment is contemplated, it should be surgical removal.

DISEASES OF THE MUSCLES AND LOCOMOTION

History. In recording the history of a complaint referable to the muscles, attention is paid to the earlier occurrence of conditions that could lead to secondary involvement of the muscles, such as acute infectious disease; for example, acute rheumatic fever, syphilis, trichinosis and diseases of the nervous system.

Direct or indirect trauma to skeletal structures is a common cause of muscular dysfunction The presence of pain and its situation, and whether the pains or the disability appeared immediately after an injury, or only some time later, may be diagnostically helpful.

Examination of Muscles. The general musculature of the patient is inspected In some the muscles have always been small; in others the muscles are voluminous. The volume depends partly on heredity, partly on the daily activity, and, most of all, on the somatic type. The mesomorphs are characteristically heavily muscled individuals

A completely absent muscle, owing to congenital defect, is rarely missed by the patient and thus no complaint is made of its absence Slight atrophy will occur whenever muscles are not used For recognition of this atrophy from disuse, comparative measurements may be required

A large part of the mass of muscles lies so near the surface that individual muscles often can be easily grasped by the palpating hand, others lie deep and are inaccessible On palpation the form of the muscle, its tone, its consistency, and whether or not it is tender on pressure are observed

A relaxed muscle feels soft, a contracted muscle feels firm Normally the consistency of a muscle is even throughout If firmer foci are felt, they are pathologic and are often due to rupture of some muscle fibers, or to abscesses, hernias, scars, gummas or tumors Free fluid or pus within a muscle gives rise to fluctuation on palpation If the testing fingers are applied in a line at right angles to the long axis of the muscle, fluctuation can often be felt in normal muscular tissue. The muscle is correctly palpated by applying the palpating hand parallel to the long axis of the muscle.

In making comparative measurements of the size of muscles in the arms or legs a steel flexible tape is employed and should be applied at exactly the same level on corresponding limbs, thus, in measuring the volume of the thigh, it is well first to draw transverse lines at distances about 4 inches (10 cm) apart above the upper margin of each patella, and then to measure the circumference at each of these levels It is well, also, to make several measurements at each level and to record the arithmetic mean A difference of less than 0.5 cm easily lies within the limits of normal variation and should be disregarded unless the difference is consistent over a considerable portion of the length of the leg or arm.

Enlargement of the muscles of a part or as a whole may be due either to true [illegible] so-called pseudohypertrophy, which

[illegible] pathologic position of the limb to which it is attached, thus a shortened biceps brachii causes flexion of the forearm, and a shortened iliopsoas flexes the hip

It is important, for instance in skin cancer, to determine whether or not the process involves the muscles or the overlying fascia. To determine this, ascertain whether the mass becomes fixed on contraction of the muscle

Hemangiosarcoma. The distinction of hemangio-endotheliomas, hemangiosarcomas and malignant types of spindle cell sarcomas is not always possible.

Hemangiosarcomas are rare tumors which develop at any age and in any part of the body. If near the surface of the body, these tumors are soft, bluish red, and may be surrounded by smaller soft nodules. Thrills are often palpated and multiple-pitched bruits may be auscultated over deeply set tumors The accurate diagnosis of these tumors is made only by biopsy.

The treatment of hemangiosarcomas is unsatisfactory by any means.

Kaposi's Sarcoma (*Multiple Idiopathic Hemorrhagic Sarcoma, Idiopathic Multiple Pigment Sarcoma*). The etiology is unknown. In some instances the lesions have followed trauma or exposure to cold. Approximately 9 of each 10 who have the disease are men The sarcoma is most commonly a disease of elderly people, although it may affect those of any age

Characteristic of this rare disease is a multiplicity of lesions. Hemorrhage occurs into the cutis, and there are deposits of hemosiderin and infiltration into the layers of the cutis. There are proliferations and formation of new and imperfect capillaries with cavernous spaces Metastasis occurs by way of lymph channels

The lesions often appear first on the hands or feet or in the region of the ankles, but they may occur in any part of the body They vary in size from 1 mm. to several centimeters in diameter and are discrete or grouped, bluish red or reddish brown, nodular discolorations. The lesions may extend along superficial veins, and often considerable edema and tenderness develop in the extremities. Localized purpura and thrombosis in superficial veins are common. Old lesions may appear to involute and leave atrophic pigmented scars. Metastasis may occur to almost any organ in the body, particularly the gastrointestinal tract, liver, lungs, and regional retroperitoneal and mesenteric lymph nodes. Some evidence indicates that the so-called metastatic lesions are multiple primary foci. In rare cases the earliest lesions may be in the viscera

The diagnosis is made by biopsy. Kaposi's sarcoma often resembles various types of granuloma, melano-epitheliomas and venous insufficiency with purpura

The prognosis is poor. The patients live from 2 to 10 years or longer Repeated roentgen treatment offers the only hope for prolongation of life

Tumors of the Lymph Vessels. Enlargement of lymphatic vessels (lymphangiectasis) is present but not apparent in all types of lymphedema and chronic lymphatic obstruction. Occasionally a dilated lymph vessel is visible, appearing as a translucent, bluish or slightly pink tubule. On spontaneous rupture or aspiration a clear or slightly yellow fluid is obtained.

Lymphangiomas comprise (1) simple lymphangioma, (2) cavernous lymphangioma, (3) *lymphangioma circumscriptum and* (4) *cystic lymphangioma*

Simple lymphangiomas are situated on skin or mucous membranes and are benign congenital tumors The *cavernous lymphangioma* is present at birth It grows slowly and is the commonest benign tumor of lymph vessels The tumors vary in size and may be [illegible] of dilated lymphatic [illegible] come [illegible] may cause enlargement of these parts, for instance, macroglossia, micro[illegible] or [illegible]omala.

Chylangiomas are cavernous lymphangiomas of the mesentery arising from the lacteals. *Lymphangioma circumscriptum* occurs in eyelids, conjunctivae, orbit, mouth, pharynx, tongue, the upper extremities, axillary or scapular regions, and in the groin or upper part of the thigh. The lesion appears as a crowded deep-seated vesicle Hypertrophy of the skin may occur over older lesions, giving them the appearance of warts, or they may be obscured by telangiectasia

Cystic lymphangiomas (cystic hygromas) are present at birth They are frequently situated in the neck, where they may grow upward toward the parotid gland and ear or downward to the axilla or to the mediastinum They may be present occasionally in the

presence of spina bifida, poliomyelitis, tuberculosis, fractures, neural or peroneal type of muscular atrophy, or muscular dystrophies is required.

Congenital Clubhand. Congenital clubhand, like congenital clubfoot, is due to maldeveloped muscles. It is observed less frequently than clubfoot

Congenital Elevation of the Scapula (Sprengel's Deformity). Abduction at the shoulder is limited since the scapula cannot be rotated. Passive rotation and active rotation of the scapula are diminished or absent because of fibrous or bony attachments between the scapula and the ribs

The affected scapula is elevated, and rotated so that its lower angle is nearer than normal to the spinal column, and the shoulder is advanced. Scoliosis and torticollis may be associated

The diagnosis is based on the forementioned findings. Roentgenograms reveal that the scapula is shortened so that the transverse diameter is relatively increased.

Congenital Contractures of the Extremities. These contractures are designated also amyoplasia congenita, multiple articular rigidity and arthrogryposis multiplex congenita Immobility of one or more joints is present as the result of absence, or incomplete development, of associated muscles

Boys and men are affected more frequently than girls and women The rigidity may affect the muscles of only one joint or the whole limb. It may be bilateral and symmetric. The commonest type of congenital contracture is that in which all four extremities are fixed in extension In some there may be fixation of the knees and the hips in flexion The whole limb commonly is slightly abducted

The affected limbs are often shortened and the range of movement at affected joints is limited to a few degrees because of muscles which are grossly defective or absent Congenital dislocation of the hips and other deformities may coexist. Roentgenograms do not reveal any bony alterations of the joints or capsules, but the muscle shadows may be very small

The diagnosis is based on the objective findings described in the foregoing paragraphs in the presence of negative results of roentgenographic examination of the joints There is little or no spontaneous improvement In severe instances surgical procedures may be helpful

HEREDOFAMILIAL DISEASES OF THE MUSCLES

The Muscular Dystrophies. The term muscular dystrophy designates a disease which is characterized by progressive wasting and paralysis of the skeletal muscles The different types of dystrophies are distinguished by the age at onset, the presence or absence of pseudohypertrophy, and the particular muscles first affected. The following forms are recognizable even if not diagnosable (1) the facioscapulohumeral type of Landouzy-Déjerine, (2) the juvenile scapulohumeral type of Erb, (3) the pseudohypertrophic type of Duchenne and (4) the femoral type of Leyden-Moebius It is abundantly clear that there is no real justification for separate descriptions of these forms

Etiology This disease may be regarded as a heredofamilial degenerative process affecting the muscles Several members of a family or their descendants are affected, or the condition often can be traced through several generations Males and females are affected alike, and either men or women may transmit the disease to their children. It has been concluded that the mode of inheritance varies in different families, and may be of at least three different types simple dominant, simple recessive, and sex-linked recessive

Pathology The muscles may be either enlarged and firm, or small and soft.

No changes have ever been demonstrated in the nervous system other than the mild alterations of the anterior horn cells and motor nerve endings which may be considered secondary In recent years it has been suggested that disturbances in the sympathetic system are to blame for muscular dystrophies, but there is still no satisfactory evidence to support this hypothesis

The tenderness of a muscle to pressure is tested by pressing portions of the muscle between two fingers rather than by pressing the muscle against underlying bone. The tenderness elicited by the latter method may be due to an inflamed periosteum and not to a tender muscle.

Spasm in skeletal muscle seems to be a reversible state of sustained involuntary contraction accompanied with muscular shortening and associated with electrical potential changes. The diagnosis of muscle spasm is often made in various types of low back pain, fractures and poliomyelitis according to Harell, Mead and Mueller who used electromyographic technics and did not find muscle spasm present in these conditions The clinical diagnosis of spasm in peripheral conditions such as backache, fracture or poliomyelitis is erroneous in a large percentage of cases.

Muscle spasm is differentiated from muscle spasticity, which is often caused by lesions of the upper motor neurons of the central nervous system. A true spasm is characterized by sustained muscular contraction. Sustained contraction or spasm is not commonly present in association with spontaneous somatic pain.

CONGENITAL DISORDERS OF THE MUSCLES

The congenital malformations of muscles consist of defects and the absence of the whole, or of part, of a muscle.

The muscular defects of greater importance are those that involve (1) the pectoralis, (2) the trapezius, (3) the serratus anterior and (4) the quadriceps femoris

These muscular defects are easily recognized by inspection and palpation of the region of the muscle, and, more especially, by functional tests

Anomalies. The origins and the insertions of muscles vary within certain recognized limits In addition to these variations, muscles may be present which have abnormal relations or attachments In an occasional individual a muscle may be present which is of no use to him but which is present in other primates as a useful muscle for example, elevator of clavicle, and sternalis and tail muscles. Vestigial muscles are often present; for example, muscles for movements of the ear and scalp

Sometimes a whole or a part of a compound muscle is lacking because of *agenesis* Almost any muscle in the body may be absent or defective, but there is a selective incidence in these ageneses and defects.

Some part of the pectoralis major or minor muscles may be absent, the sternocostal part of the pectoralis major is that most commonly lacking The trapezius, quadriceps, [illegible] sterno-

[illegible] ntly present In rare instances several members of a family may present the same peculiarity of absence or defects of muscles

Congenital Clubfoot. *The deformities of the feet which are of congenital* origin are talipes equinus, the plantar flexed foot; talipes calcaneus, the dorsally flexed foot; talipes varus, the inverted and adducted foot; and talipes valgus, the everted and abducted foot The commonest type, however, is talipes equinovarus, in which the foot is plantar flexed and inverted. In most instances the condition is bilateral

Macklin stated that this condition is inheritable and dependent on a recessive *factor* or on multiple factors and since most of these patients are males, a sex-linked factor is suspected The deformity often occurs in otherwise healthy babies

In the common type of talipes equinovarus the foot is inverted and flexed so that the plantar surfaces of the two feet may be brought into contact The attempt to manipulate the foot into normal position is resisted by the ligaments and by the shortened tibial muscles. The tendons are displaced, the shortened muscles are fibrotic and atrophied, and the bones of the ankle and foot have come to be deformed as the result of growth in the malpositions imposed on them.

The diagnosis is obvious. Differentiation from acquired clubfoot caused by the

Myotonic Dystrophy (Myotonia Atrophica) This is a rare type of heredofamilial degeneration of selective atrophy of muscles, myotonia, cataract, alopecia, atrophy of the sex glands, and premature senility The condition is generally regarded as an independent disease, although it appears to bear some relation to myotonia congenita and to the muscular dystrophies (Ford).

The onset of symptoms is usually between the ages of 20 and 35 years, but it may occur in childhood The first symptoms may result from wasting of the muscles or from myotonia. The muscles which are first attacked are the facial, especially the orbiculares of the eyelids and the mouth, the masseters and temporals, the sternocleidomastoids, the extensors of the forearms, vasti of the thigh, and the dorsiflexors of the feet. In some cases the tongue, soft palate, pharynx and vocal cords are affected Speech is characteristically low-pitched, monotonous and often nasal The hard palate is very high and narrow, and the face is long and thin These patients are usually dull in mentality and are often definitely feeble-minded

The myotonus is always present It is easily elicited by having the patient grip the examiner's hand with maximal force and then open the fingers as rapidly as possible. It will be seen that the flexors do not relax for a second or more after the extensors begin to contract There may also be difficulty in opening the eyelids after closing them tightly, cramping of the feet on attempting to run, and stiffness of the jaw muscles when chewing. Often repetition of the movement several times will result in disappearance of the myotonus Sudden falls may occur as a result of general myotonus, provoked by an effort to run or by an emotional stimulus.

Ford observes that when there is characteristic distribution of the muscular wasting, the myotonus, the cataracts, the characteristic baldness, the testicular atrophy, and the appearance of premature senility distinguish this disease from the muscular dystrophies, and in the presence of these findings the diagnosis is certain.

The disease is incurable but may permit of survival for many years, for in many cases it progresses very slowly

Myotonia Congenita of Thomsen. This is a heredofamilial disease which becomes apparent very early in life, and is characterized by a tendency to myotonia and often by a bulky musculature as well as by various mental disturbances. The cause is unknown The disease is usually present in several members of a family, and may be traced through a number of generations. It affects males and females alike, and may be transmitted by either sex. This disease may behave as either a dominant or a recessive characteristic

The onset is in childhood It is not unusual for the symptoms to increase in severity about the age of puberty The first symptom complained of is an inability to let go quickly of an object which has been grasped firmly. When the patient suddenly rises or starts to run, the muscles become rigid, so that the patient may be unable to take a step for some seconds, or may even fall helplessly to the ground. After the movement has been repeated several times, the rigidity slowly wears off, and the patient then is able to contract and relax the muscles normally. A sudden fright, a loud or an unexpected noise, great anger or mental distress is almost certain to produce general rigidity in affected persons. Cold weather also accentuates the myotonia

The myotonus may be found only in the legs or in the arms. The facial, ocular and tongue muscles may be affected Myotonia may be active or latent Latent myotonia may be elicited only by percussion, by electric stimulation or by causing the patient to sneeze (use snuff). In some patients, emotional reactions are the most effective stimuli.

The muscles are almost always bulky, even suggesting a mesomorphic somatic type or hypertrophy. Strength and endurance are not diminished, and it is possible for these patients to take long walks or to dance for hours

When atrophy is the main lesion of the muscle, there may be resemblance in the findings to those present in lower motor neuron lesions A discussion of these relationships is to be found under Lower Motor Neuron Lesions, p. 331.

SYMPTOMS. The insidious onset may occur at any time during childhood. The parents usually complain that the child has a clumsy gait, that there is difficulty going upstairs, and, not infrequently, it is noticed that the abdomen is unduly prominent. The essential symptoms include progressive weakness and wasting of certain muscle groups. first the muscles of the shoulder girdle and the pelvic girdle, and later the muscles of the upper arm and the thigh. The wasting may or may not be preceded by pseudohypertrophy.

EXAMINATION As a result of weakness of these muscle groups a number of clinical signs may be elicited which are characteristic of the dystrophies. Weakness of the muscles which fix the scapula, namely, the serratus magnus, trapezius and rhomboids, results in winging of the scapula or displacement of the vertebral border of the scapula from the thoracic wall so that it stands out like a wing whenever the patient attempts to elevate the arms

As a result of weakness of the pelvic girdle and hip muscles the patient, usually a child, stands with the pelvis tilted forward, abdomen and buttocks protuberant, and a marked increase of the lumbar lordosis. In walking, the trunk is swung from side to side as a result of weakness of the abductors of the thighs, chiefly the glutei medii. The gait is not unlike that of double congenital dislocation of the hip. Children who can walk fairly well on level ground experience great difficulty in going upstairs or stepping upon a chair. In getting up from the floor the child turns over on the face, draws up the knees and gets up on the hands and knees Next, the legs are extended so that the child is resting on hands and feet with bent knees. The last maneuver is to work the hands back to the legs and, by grasping the legs at higher and higher levels, to push the trunk erect by the arms When the process extends below the knees, the dorsal flexors of the ankles are affected before the extensors, so that the foot is maintained in the equinus position The knee jerks are lost early, but the ankle jerks persist until late in the course of the disease Severe contractures often develop, especially in the flexors of the hip and the extensors of the ankles, and even deformities of the bones may occur from the long-standing loss of muscle balance. Sensory disturbances are absent, and there is no disturbance of sphincteral control In uncomplicated cases there are never any fibrillary or fascicular twitchings

The rate of excretion of creatine is abnormal in adults In all patients who have muscular dystrophy the rate of excretion of creatinine is normal or increased.

The roentgenologist may recognize a conspicuous streaking of the soft tissue shadows of affected muscles There is a delayed appearance of centers of ossification in the epiphyses of the long bones and in the bones of the hands Demineralization of the bones may be observed

DIAGNOSIS The diagnosis of muscular dystrophies is usually obvious However, there may be difficulty at times in differentiating Werdnig-Hoffmann muscular atrophy, amyotonia congenita, progressive neuromuscular atrophy, amyotrophic lateral sclerosis and polyneuritis The course is usually very slow, and many patients survive for 10 to 30 years after the onset of symptoms.

Muscular dystrophies occurring in men and women between the ages of 40 and 55 years may be observed The women are often beginning the menopause at the time of onset. In these there is no genealogic history of similar affections.

The disease begins by weakness and shrinkage in the size of the affected muscles. The manifestations may be of the facioscapulohumeral type, or the face and the shoulder girdle may escape and the muscles of the buttocks and thighs be largely affected In rare instances there is a hyperfunctioning of the thyroid gland.

In some instances the disease progresses to a fatal termination; in others, the symptoms may become arrested, or there may be improvement or even partial recovery.

Epidemic Myalgia. The disease is known also as pleurodynia, devil's grip and Bornholm disease The etiology is unknown. The disease occurs in epidemics and affects children and young adults. The disease seems to spread by contact, and it is not unusual for all the children in a family to be attacked at the same time. The incubation period seems to be between 2 and 4 days.

Pain develops in the muscles of the back, shoulders, abdomen and hips. Pain in the muscles of the thorax and the diaphragm is the first and often the most prominent symptom. There is pain on inspiration, and consequently respiration is shallow and rapid The pain is present also in the muscles of the back, shoulders, abdomen and hips. The more acute pain lasts as a rule only 1 or 2 days, but tenderness may persist somewhat longer. There is only slight fever. Hiccough is present in some cases.

The affected muscles are tender to pressure. There may be localized swellings There is mild leukocytosis and an excess of eosinophils. In the presence of complications there may be found a dry pleurisy, pneumonia and otitis media. Orchitis is occasionally present.

The diagnosis cannot be made except during an epidemic The differential diagnosis comprises the consideration of pleurisy, appendicitis and dengue fever.

Relapses occur in almost one fourth of all cases, and second attacks are common The disease is never fatal, and there are no residua

Dermatomyositis. This is an acute or subacute inflammation of the muscles associated with edema and dermatitis which usually terminates fatally. The involvement of muscles is widespread, it consists of muscular firmness and stiffness, proliferation of interstitial tissue and fatty degeneration.

The disease commences with stiffness, soreness and tenderness of the muscles of the extremities. The trunk muscles may be involved early. The skin over the affected muscles is edematous and often contains erythematous, urticarial or erysipelatoid eruptions. Loss of sensations of the skin is common

The course of the disorder is rapidly progressive, it is fatal in 1 to 3 months and death often follows involvement of the muscles of deglutition or respiration. If recovery should occur, atrophy of the muscles ensues.

Tuberculosis. The contractile tissues of muscles rarely show tuberculous lesions, so that one may speak of an "immunity" of muscles to tuberculosis

Parasitic Infections. These include (1) trichinosis, (2) echinococciasis of muscle and (3) cysticercosis of muscle These conditions have been described in connection with the respective parasites The diagnosis is established by muscle biopsy

TRAUMATIC DISEASE OF MUSCLES

Sudden and violent stretching of a muscle may produce rupture of a tendon or a muscle This causes acute pain The ruptured belly of the muscle may be displaced in the direction of the remaining attachment, and when the muscle contracts, the displacement becomes more evident The muscle exerts no motor effect, but can be seen to contract voluntarily Rupture of the tendon of the long head of the biceps is perhaps the commonest rupture of a tendon In the same way the belly of the muscle may be torn Rupture of the plantaris muscle is apparently not very rare and may occur without violent exertion In some cases violent exertion may cause rupture of the sheath of a muscle A muscle hernia develops as a result, which disappears when the muscle contracts The groove resulting from rupture of the muscle may be palpated. When the muscle contracts, a swelling appears on either side of the groove.

The diagnosis is not difficult if the myotonia is elicited. This condition rarely causes severe incapacity and does not progress. Wolf has shown that quinine will abolish the myotonus of myotonia congenita.

Sleep Paralysis (Dead Asleep) Sleep paralysis is frequently associated with narcolepsy, and attempts by some patients to ward off an attack precipitate an attack of helplessness However, sleep paralysis accompanying natural sleep is a benign condition, probably resulting from a dissociation of the components of sleep. It should be differentiated from familial periodic paralysis. The patient is assured that although the disorder is alarming it is always of short duration and does not result in permanent paralysis or any other disease. Usually just a slight touch suffices to dispel sleep paralysis.

INFECTIONS OF MUSCLES

Intramuscular Abscesses. Acute pyogenic infections of muscles usually result from (1) extension of an infection from the skin above or the bone below, (2) the lodgment of bacteria or infected thrombi or (3) necrosis of tissue and formation of abscess from intramuscular medications.

The symptoms of an intramuscular abscess are pain, swelling, redness and increase in local temperature. Fever often is present There is often a fluctuant mass below the skin and subcutaneous tissue.

The diagnosis is usually obvious, for almost all of these abscesses result from intramuscular medication. The history and the findings are definite.

Local Myositis. Local myositis is often a complication of acute rheumatic fever and is then known as rheumatic myositis. In the acute stage the inflammatory exudate in the muscle can be felt as a firm mass. Later on, this may be followed by the formation of scar tissue (chronic myositis) or by atrophy of the muscle

Gonorrheal myositis may be associated with gonorrheal arthritis. The muscles near the affected joints are most often affected. Occasionally *syphilitic myositis* is met with, in the form of an infiltrating inflammation or of a gumma The so-called *myositis fibrosa* is an end stage of various forms of acute myositis (infectious, traumatic, parasitic). Local ossification of muscle may occur occasionally

Nodular Myositis. Nodular myositis often is present in rheumatoid arthritis. However, nodular myositis is a comparatively common condition in a wide variety of diseases and it is of no diagnostic value in cases of rheumatoid arthritis

Myositis Fibrosa. Myositis fibrosa is a subacute or chronic inflammation of the muscles occurring either locally or generally. It is associated with slight constitutional symptoms, and eventually ends by the replacement of the muscle fibers by connective tissue However, there are many similarities between myositis fibrosa generalisata and progressive muscular dystrophy. The former is essentially a degenerative and not an inflammatory lesion of the muscles. It is not a separate clinical and pathologic entity but is one form of progressive muscular dystrophy.

Disseminated foci are found in which the muscle fibers are undergoing hyaline and vacuolar degeneration. The blood vessels are thickened

The disease begins in the thighs or calves by shortening and inelasticity of the muscles, so that movements are limited in range There are no constitutional reactions such as are observed in dermatomyositis. Gradually the muscles of the hips, abdomen, spinal column, thorax and neck are involved The arms and face are usually affected very late. In some cases the process is generalized and symmetric and is diagnosed *polymyositis*. It may occur asymmetrically and locally.

The physical examination in the beginning reveals an extra firmness of the affected muscles In advanced stages of the disease there are contractures which fix the body and extremities in a position of flexion. The tendon reflexes of the affected muscles are diminished or lost No reduction of sensibility is found The diagnosis is based on the results of biopsy studies

Myasthenia gravis is characterized by weakness and by abnormal fatigue of the striated muscles which is not constantly associated with any demonstrable anatomic lesions.

PATHOLOGY. In some instances the thymus is found to be abnormal, although the abnormality is neither constant nor specific. The thymus may be enlarged; it may be small, degenerated and cystic; or it may have undergone neoplastic changes. The neoplastic change has the appearance of a lymphosarcoma No definite lesions have been demonstrated in the muscle fibers or in the nervous system

Myasthenia gravis occurs at all ages Ford recorded an infant of 18 months who had the disease. There is no evidence of morbid heredity

SYMPTOMS In many cases the symptoms of myasthenia gravis are manifested without apparent cause, and in many others the disease follows a respiratory infection such as influenza or bronchitis.

There are abnormal fatigability and weakness, and finally paralysis of the striated muscles As a rule the muscles innervated by the cranial nerves are affected first, and often dysphagia may be a presenting symptom. Often, however, diplopia is the first symptom, which may accompany or be followed by the appearance of ptosis of one eyelid or both eyelids and by some limitation of ocular movement. The patient may complain of being unable to look up, and thus upward rotation of the eyeball is limited before any other movement is impaired The palsies of fatigue do not correspond to the distribution of any single nerve The pupils react normally. In the morning the patient is refreshed and more alive than at any other time of the day As the day passes, the lids droop and by evening the patient cannot hold the eyes open sufficiently to walk safely Weakness of the bulbar muscles commences shortly after the ocular muscles begin to tire. The voice becomes weak, and persistence in talking results in a nasal and hoarse voice

EXAMINATION Mental alertness is maintained Muscular weakness, as implied by the symptoms, is revealed on examination The jaws grow tired when the patient chews. The face is relaxed, the eyelids cannot be firmly closed, and the corners of the mouth droop The neck grows weak relatively early in the course of the disease and may become so weak that the head cannot be lifted from the pillow. Weakness of the bulbar and oculomotor muscles can be demonstrated before the extremities are affected. The patient eventually becomes too weak to walk or stand The tongue cannot be protruded and articulation is difficult or impossible At this stage of the disease respiration becomes difficult Death may result from failure of respiration within a few hours Except for the muscular atrophy due to disuse, none is present which can be determined with certainty

The muscles are atonic and soft The tendon reflexes are reduced, or abolished, in those who have advanced weakness. In all instances of the disease the tendon reflexes are usually normal at first, but on repeated elicitation the muscle becomes fatigued and finally the reflexes disappear The heart muscle and smooth muscle are not affected at all or only to a very limited extent. Neither the special senses nor other modalities of sensibility are altered in any way

The abnormal excretion of creatine in the urine and the diminished excretion of creatinine are regarded as secondary effects of loss of muscle function since these findings are present in other diseases affecting the muscles Hypoglycemia too must be regarded as secondary

An enlargement of the thymus can be demonstrated in some instances on physical examination or roentgenologic examination. Enlargement of the thymus has been considered etiologically important by Eaton

DIAGNOSIS A diagnosis of myasthenia gravis can be made when there is a definite abnormal weakness of the striated muscles, usually beginning in the ocular or bulbar muscles, and finally becoming generalized, provided there have been remissions and exacerbations of the weakness The abnormal weakness of the muscles is

The history and the findings are diagnostically conclusive.

As the result of direct trauma all or a part of a muscle may be ruptured. For instance, a part of the quadriceps femoris muscle is often ruptured from the trauma of falling forward and astride the steering wheel of an automobile when the overturning car comes to a sudden stop.

HERNIA OF MUSCLE

Hernia of a muscle, due to a defect in the aponeurosis that permits a mass of muscle to bulge through it on contraction, may follow trauma, but it often results from congenital fascial defects

Hernia of a muscle is diagnosed by observing and palpating the muscle during voluntary contractions.

Fascial Hernias of the Legs. Fascial hernias of the legs occur unilaterally and bilaterally in the muscles of persons whose legs have been exposed to severe chronic strain, such as athletes, skiers, mountain climbers, foresters and foot soldiers who have exercised in hilly or mountainous country.

CONTRACTURE OF MUSCLES DUE TO CIRCULATORY DISTURBANCE

Volkmann's Ischemic Contracture. The most serious and one of the commonest types of traumatic injury from ischemia is Volkmann's ischemic contracture However, comparable contracture may occur as the result of circulatory disturbances in compressed, injured muscle in any part of the body

It is generally accepted that circulatory disturbances are responsible for ischemic contractures In Volkmann's contracture the application of tight splints is usually held to blame However, hemorrhage and edema under the fascia in the antecubital space could compress and obstruct the blood vessels there and produce the contracture even if a cast to the arm had been originally correctly applied. The application of a tourniquet or occlusion of the large vessels of the arm may cause the contracture

In Volkmann's contracture there is at first edema, followed by necrosis of the muscle fibers. The fibers are gradually broken down and replaced by connective tissue. The muscle becomes a mass of scar tissue which is adherent to the skin, the tendons and bones.

Volkmann's contracture is found almost exclusively in the muscles of the forearm which flex the fingers and wrist. It follows severe injury to the region of the elbow joint, such as fracture of the lower end of the humerus or of the bones of the forearm. Application of casts which are too tight, a cast made too tight after application by hemorrhage under the fascia, and occasionally application of a tourniquet are the common causes of ischemic contractures Ischemic contracture is very painful and is characterized by pronounced swelling and cyanosis of the fingers

On examination the fingers are cold and blue. Later the skin is drawn tight and is adherent to the subcutaneous tissues and shrunken muscles. The fingers and perhaps the wrist are flexed so strongly at the distal joints that the nails may press into the palm, but the proximal joints are extended. The thumb may or may not be affected. The atrophy and induration are mainly of the extrinsic and intrinsic flexors of the hand and fingers

The diagnosis in the fully developed condition is obvious If the condition can be recognized before irreparable damage is done, the splints should be removed at once. If the circulation does not improve satisfactorily, an incision should be made into the antecubital space and the blood clot removed The prognosis is bad.

TOXIC AND METABOLIC DISORDERS OF MUSCLES

Myasthenia Gravis. Synonyms for myasthenia gravis are asthenic bulbar palsy, bulbar palsy without anatomic basis, myasthenia gravis pseudoparalytica and Goldflam's disease.

The Tic Diseases. A tic is a co-ordinated muscular movement that has become imperative, a functional disorder. The movement may correspond to that of a reflex, defensive or expressive type. The tic is response to an irresistible impulse to movement which makes the patient uncomfortable until the action is performed. It is brief, may be violent, repetitious, and limited to a single movement, or it may be characterized by a multiple series of movements.

Isolated Tics. These tics are commonly present in the facial muscles and represent specific acts such as sucking, licking and biting Scratching and rubbing, particularly of the nose or face, may represent a tic.

Generalized Tic. The disease commences as a form of facial tic—blepharospasm, or *distortion of the mouth—or with a head-nodding tic. Later, stereotyped* tics in the extremities appear Practices without reason or emotional urge are indulged in, such as grabbing of the nose, pulling the chin, or throwing the head to the side, hand-clapping and foot-stamping. In some instances the tics seem to be part of a psychasthenic state, in others, of a dementia praecox. A generalized tic once manifested does not stop.

Generalized tic is distinguished from Sydenham's chorea, from hysteria and from double athetosis These patients are usually schizophrenics.

Paramyoclonus Multiplex. The disease is known also as myoclonia, polyclonia and Friedreich's myoclonus The clonic contractions cause short, quick jerks of the extremities, not involving synergistic muscle groups, and varying in number from a few to 100 per minute. The muscles often involved are the brachioradialis, biceps, trapezius, quadriceps femoris and semitendinosus The contractions disappear in sleep The deep reflexes are exaggerated

The disease must be differentiated from the tic diseases, hysteria, petit mal and chorea chronica

Writers' Cramp. Persons of various occupations are prone to a disturbance of special, skilled, co-ordinated muscular movements used in performance of their work.

Writers' cramp develops in psychoneurotic patients The disturbance commences with an abnormal fatigability on writing; later there is a feeling of cramp in the muscles The writing becomes abnormally irregular, almost illegible, especially when the writer is under observation Results of physical examination of the nervous system may be negative except for the presence of psychoneurotic signs.

Writers' cramp is distinguished from agraphia, paralysis agitans, hemiplegia, tabetic ataxia beginning in the upper extremities, familial and acquired intention tremor, and multiple sclerosis

TUMORS OF THE MUSCLES

Tumors of muscles may be benign or malignant The benign tumors include lipomas, fibromas and osteomas The malignant tumors include, as primary tumors, angiomas and sarcomas, and sometimes, as a secondary tumor, carcinoma. Tumors of muscles should not be confused with myositic indurations, tuberculosis, gumma or parasitic invasions

Desmoid Tumors of Muscles (Fibromas). A desmoid tumor may be defined as a very hard tough fibroma Multiple desmoid tumors may occur in striated muscles, especially in the anterior abdominal wall However, these tumors either singly or multiply occur elsewhere in the body.

That these tumors are due to trauma (accidental, operative, or the physiologic trauma), combined with an unknown individual predisposing factor, appears to be the most logical theory of origin These tumors do not undergo metastasis nor do they endanger life, however, they do tend to recur locally *Diagnosis is made by* finding a fibrous tumor in a muscle, the tumor is fixed by contraction of that muscle. Biopsy is indispensable for diagnosis.

revealed by an increase of symptoms in the evenings and by fatigue in repetition of movements of affected muscles. An improvement in the symptoms which follows the injection of neostigmine (prostigmin) is of diagnostic value, for such always occurs in myasthenia gravis, and never so dramatically is improvement witnessed in other conditions Myasthenia gravis is rare in childhood, and in this period the diagnosis must be made with caution

Quinine sulfate will precipitate the symptoms of myasthenia gravis. Curare in very small doses is used as a test for myasthenia gravis. Patients who have this disease are very sensitive to curare and for this reason this drug should not be used by those who have not had supervised experience in its use When curare is used as a test for myasthenia gravis not more than one twentieth of the curarizing dose is employed The test is positive if great muscular weakness is produced by the administration of curare

There is no curative treatment at present. Prostigmin (5 to 15 mg doses) is of great value but its effect is purely symptomatic. The effect of each dose lasts about two hours

In some instances the symptoms advance rapidly and death supervenes within a few months In others, in which symptoms are definite, there is a tendency for them to remain stationary for a long period. In some instances there are recurrent exacerbations with complete remissions between.

OSSIFICATION IN MUSCLES

Hematomas and granulation tissue resulting from inflammatory processes in muscles may eventually become ossified. Bits of periosteum torn from the bones as a result of trauma give rise to formation of new bone Long-continued trauma of a milder type may also lead to bony deposits in the muscles or tendons For example, plaques of bone are found in the adductors of the thighs in individuals whose occupation requires daily horseback riding Extensive bony processes sometimes appear in the muscles of the lower extremities in severe spastic paraplegias of long *duration. These conditions are localized and do not progress beyond local limits.*

Progressive Myositis Ossificans. Progressive myositis ossificans is a generalized ossification of the skeletal muscles which is dependent on some inborn defect. The etiology is unknown (see also page 1535)

In the beginning there is muscle edema, and often there are hemorrhages The onset begins before the tenth year There is a local, firm, nontender swelling situated in the muscles of the trunk or back of the neck The skin may be slightly red and tender The swelling slowly disappears, leaving a firm small region in the muscle which eventually becomes bony In time successive swellings develop, leaving a bony deposit.

When the disease is fully developed, it can scarcely be confused with any other condition The roentgenographic appearances are characteristic.

In those who survive long enough the disease progresses sufficiently to produce invalidism and death from inanition or fixation of the respiratory apparatus

MUSCULAR DISORDERS SECONDARY TO DISTURBANCES OF INNERVATION

These disorders include (1) the muscular atrophies due to lesions of the lower motor neurons and peripheral nerves, (2) the muscular atrophies due to disuse and

[illegible]

otor neurons and peripheral

ies of muscles from disuse

occur when a joint is mobilized as by a plaster cast or ankylosed

The hyperkinesias comprise the tic diseases, choreas and the occupational neuroses.

wasting, small groups of muscle fibers show irregular twitchings known as fibrillary twitchings or fasciculation. The degenerating muscle is usually extremely tender to pressure and may be painful and subject to cramps.

During this phase of degeneration in the muscle it may show what is known as the reaction of degeneration. The electric testing of muscular reactions is of no value unless performed by an experienced hand, and it is comparatively rare for this testing to provide diagnostic information that cannot be obtained by other means Of greater diagnostic importance is the fact that apparatus for such testing is not usually available in practice.

It is immediately apparent that *lesions of the lower motor neuron* and the neural or *peroneal muscular atrophy* have symptomatically much in common. A neural or peroneal atrophy is characterized by a slowly progressive palsy with flaccidity of muscles. A *hypertrophic interstitial neuritis* causes the same symptoms but can be recognized by the palpable thickening of the peripheral nerve trunks. In either disease more than one member of a family may be affected

In the descriptions of the diseases of the muscles it was recorded that the *myopathies* are characterized by chronic and progressive wasting of the muscles and frequently appear in several siblings. The muscles of the pelvic girdle and the shoulder girdle are selected by this process and the muscles of the proximal parts of the extremities are also affected early in the course of the disease.

Muscular atrophies and flaccid paralysis are due either to a lower motor neuron lesion or to lesions in the nerve or the muscles. When the lesion is situated in the muscle, it is comparable to the lesions present in the muscular dystrophies. The muscles are soft, waste away, and throughout the illness lack tone There is absence or diminution of the tendon reflexes The plantar response is flexion. When the lesion is in the lower motor neuron, tests of electric excitability reveal loss of faradic reaction and a slow galvanic response, that is, the reaction of degeneration. When the lesion is in the muscles, there is only a quantitative reduction of irritability. Atrophy of the muscles must be distinguished from defective development When the lesion is situated in a peripheral nerve trunk there are muscular atrophy and sensory changes in the skin.

Among the *congenital conditions* giving rise to a generalized chronic congenital weakness and loss of tone of the muscles are amyotonia congenita and atonic cerebral diplegia. Both of these diseases are uncommon

Among the conditions causing flaccid paralysis at birth are rupture or stretching of the brachial plexus during birth which frequently causes paralysis of the fifth and sixth roots of the plexus with loss of abduction and external rotation at the shoulder, of flexion at the elbow and of supination of the forearm. Injury to the upper roots of the brachial plexus during birth may cause paralysis of the diaphragm on one or both sides

Because of the high incidence of local palsies with atrophy, as the result of injury to the spinal nerves, these are always considered in any diagnosis when these findings are present The nerve may be lacerated by fragments of bone, injured by pressure of a tight splint or compressed by formation of scar tissue or callus Falls which depress the shoulder may cause brachial plexus palsy.

Acute Anterior Poliomyelitis (*Infantile Paralysis, Heine-Medin Disease*) Poliomyelitis is an acute infectious disease that is caused by the smallest in size of the filtrable viruses which has sufficiently distinct properties to permit its identification with much certainty.

There are three immunologically distinct types of the poliomyelitis virus: type 1 (Brunhilde), type 2 (Lansing) and type 3 (Leon). These types are so sharply

Venous Angiomas of Skeletal Muscle. In some patients angiomas of the muscles are true tumors. They may grow and exhibit the characteristics of a malignant neoplasm. In others angiomas are malformations, masses of swollen blood vessels which are of congenital origin or clearly related to injury. Their course is variable; many remain stationary; some disappear spontaneously. The angiomas of congenital origin do not produce symptoms until late childhood or early adult life

Venous angiomas of skeletal muscle occur with about equal frequency in the two sexes In most cases the malformation is first observed during childhood or early adult life

The symptoms commence with pain and swelling related to muscular movement. The tumor and thus the symptoms may occur in any striated muscle, although the most frequently involved muscle seems to be the quadriceps extensor. Venous angiomas vary in diameter from less than 1 inch (1 to 2 cm) up to 4 or 5 inches (10 to 12 cm.) or more.

Paresthesias, numbness and periodic or constant swelling are commonly present There is occasionally fixation of the overlying skin which exhibits some degree of bluish discoloration The mass is soft and movable; rarely is it firm and fixed. Seldom are pulsations or *bruits to be made out unless there are free arteriovenous com*munications

In addition to the clinical examination there are three procedures which are diagnostically helpful (1) exploratory puncture, with aspiration of normal blood, (2) the intravenous injection of radiopaque solution, and (3) roentgenologic examination *The diagnosis is based on the history and the findings on examination*

LOCOMOTION AND THE NERVOUS SYSTEM

In man the basic structures subserving locomotion, consisting of bones, joints, muscles and nerves, have not changed greatly since he began to walk on his hind legs. The great change has come about through freeing the front quarters of their main responsibility in locomotion. The front quarters, having been emancipated from responsible locomotor functions, come more under the influence and guidance of the cerebral cortex than do the front quarters of the animals who use them solely for locomotion. It therefore has been necessary to consider the organization of the motor nervous system as such after the description of the diseases of locomotion as they occur in bones, joints, muscles and peripheral blood vessels.

The neuron concept of the development and structure of nerves and nerve fibers repudiates the idea that nerve fibers develop from cell chains or a syncytium, and holds (1) that all axons and dendrites are true outgrowths from nerve cells and (2) that each neuron remains throughout life a discrete structural and functional unit Critical cytologic observations favor discontinuity where process and cells of different neurons come into functional contact Collateral evidence is afforded by the behavior of neurons after severance or injury, the fibers distal to the point of section (and thus isolated from their cell bodies) degenerate, whereas the central stumps live and regenerate

THE MOTOR NERVOUS SYSTEM

On the basis of structure and function, the motor nervous system is divided into five components, namely, (1) the lower motor neuron, (2) the upper motor (pyramidal) neuron, (3) an extrapyramidal system of neurons, (4) the cerebellar system and (5) the frontal cortex (eupraxic functions) *immediately anterior to the* motor cortex.

The Lower Motor Neurons and Locomotion. Any lesion which interrupts the lower motor neuron deprives a muscle of its nerve supply and causes it to become flaccid and completely paralyzed, to lose its tendon reflex and to waste. Fibrous changes take place in its structure, *it shortens and undergoes contracture.* In cases in which the interruption of nerve supply is incomplete during the active process of

are no data to support a contention that dietary deficiencies predispose to poliomyelitis. On the contrary, it often seems that the victim of poliomyelitis is well nourished, perhaps even better nourished and developed than the children who do not get the disease.

PATHOLOGY Focal areas of injury are present in the pons, brain stem, motor cortex and meninges Injuries have been found in the dorsal root ganglion There are irritation and hyperplasia in mesenteric and enteric lymphatic tissue which are especially conspicuous in children

In the spinal cord the lesions are most prominent and extensive in the cervical and lumbar enlargements, especially in gray matter of the anterior horns. It is the destruction of ganglion cells in these areas that is responsible for the clinical expression of the disease. Pathologically the disease is associated with destructive lesions in the gray matter of the spinal cord and brain, the white tracts being largely spared

Depending on the severity of the disease process or the situation of the main involvement in the spinal cord, several types of poliomyelitis have been designated In the *abortive* type there are constitutional symptoms without symptoms of invasion of the central nervous system. In the *nonparalytic* or *meningeal* type there are constitutional symptoms of the abortive type plus fever, drowsiness and signs of meningeal irritation and an increase of cells in the spinal fluid No paralysis occurs in these cases. The *spinal* type embraces the classic forms of the disease When symptoms indicate involvement of the medulla, pons or midbrain occurring alone or combined with spinal symptoms, the disease is designated the *brain-stem* type.

SYMPTOMS In most instances of poliomyelitis the first symptoms are referable to the gastrointestinal and respiratory systems singly or combined There are fever, headache, catarrhal inflammation of the respiratory passages and often diarrhea The temperature reaches its peak in the afternoon, 100 to 103 F (37.7 to 39.4 C), and shows a tendency to drop in the morning In from 1 to 3 days symptoms referable to the central nervous system appear. In a few cases a remission follows the initial symptoms Then the temperature rises again and paralysis may or may not supervene. An occasional case of poliomyelitis is observed without initial symptoms and is characterized by an abrupt appearance of paralysis.

Headache is the most distinctive initial complaint in poliomyelitis. This is usually of a severe, generalized, unrelenting type, which is a rare symptom in the illnesses of childhood In addition to headache and fever there are nausea, vomiting, anorexia, stiff neck, stiff back, painful extremities and general malaise with listlessness The muscular pains may be severe Sore throat may be an early complaint. The absence of inflammation of the throat in patients who complain of sore throat suggests the possibility of a painful throat of neuritic origin The complaint of sore throat occurs more frequently in those in whom bulbar paralysis develops than in other patients. There may be drowsiness and apathy Irritability alternating with drowsiness is common Sometimes the drowsiness deepens into stupor or in fatal instances into coma Within a short time signs and symptoms indicative of involvement of the segmental motor apparatus develop. The fever lasts for 4 or 5 days and falls by lysis, although it may persist for several weeks The prostration and drowsiness may continue for several days after the fever has ceased

In the cerebral type there is a profound stupor, both with and without spinal palsies Included here also is hemiplegia, the type with an acute febrile onset without spinal palsies (Strumpell's polioencephalitis).

The paralysis remains unchanged for several weeks before improvement commences. The major part of the improvement may be expected within six months, but appreciable returns of tone and muscle power may be observed after the end of the first year. There is atrophy of the affected muscles on the permanency and extent of which depend the spinal lesions The paralysis of groups of muscles imposes the additional handicap of lack of muscle balance. The soft bones of childhood are unable to cope with a lack of balance to carry the body weight, and the ankles,

defined that convalescent serum from one type will not protect against the others and also that the convalescent monkeys which are immune to reinoculation with one type can be reinfected with another type. Many observers believe that in the human being the virus of poliomyelitis is distributed *predominantly in only two systems, the* nervous system and the alimentary tract.

In human infections probably the virus enters the body by way of the mouth and establishes itself throughout the alimentary tract, where *it proceeds to multiply* There is suggestive evidence that the walls of the pharynx and small intestine are among the chief sites of virus multiplication while the virus is in the alimentary tract, and that the feces are the chief means of virus elimination The *virus may begin its* invasion of the central nervous system along the *cranial nerves that supply the* upper part of the digestive tract and thus pass into the medulla. It may enter by way of the parasympathetic system along the vagus from the middle part of the digestive tract into the spinal cord It could pass along the visceral afferent fibers through the *spinal* ganglia or along the visceral efferent fibers from the intestine by way of the abdominal sympathetic ganglia.

Poliomyelitis is cosmopolitan in distribution It occurs in epidemic, sporadic and endemic forms No *race is immune. In the United States it is most prevalent in* Vermont, New York, New Jersey, Nevada and Minnesota. More than three fourths of the sporadic cases occur between June and October, and all the epidemics have prevailed during the warm months of the year

The *disease is contagious,* being transmitted directly by droplet infection by healthy carriers of the virus, by those who are in the prodromal stage, or by those acutely ill with the disease

Children between the ages of 2 and 4 *years are most susceptible to poliomyelitis;* the disease is unusual in early infancy and in adult life. In no age group, however, is there full immunity Blood serum of convalescents, and of many adults who are not aware of ever having had poliomyelitis, contains antibodies, thus indicating that the morbidity rate is much higher than is recognized from the clinical evidence of having had the disease. A high degree of immunity is conferred by an attack of poliomyelitis, since second attacks are exceedingly rare.

The incubation period varies between 7 and 14 days, and often from 1 to 6 days. In Casey's experience the incubation period (calculated from exposure to onset of prodromal period) in 37 instances of epidemic human poliomyelitis varied from 5 to 35 days and averaged 12.2 ± 1.1 days

Casey, Fishbein and Bundesen observed that *multiple cases of poliomyelitis in the family* are the rule rather than the exception when there are other children from about 2 to 9 years of age in the home The disease is less infectious in the older groups. In many instances of poliomyelitis, the disease was so mild that a physician was not consulted Once the disease is present in a neighborhood, there is no evidence that flies and other insects play a major role in the spread of the disease.

Cunning presented a statistical report which completed a four-year nationwide survey conducted by the American Laryngological, Rhinological and Otological Society. This study was based on 36,678 cases of poliomyelitis and 96,379 cases in which *tonsillectomy* had been performed. It failed to reveal any causal relationship between poliomyelitis and tonsillectomy The studies did not indicate that tonsillectomy should be indefinitely postponed in the summer months simply because poliomyelitis is prevalent during this season. The author did not, however, advise operation during any epidemic, regardless of its nature

Clinicians generally agree that a deficiency in vitamins or other essential food elements usually results in a lowered natural resistance to bacterial infections. There is reason to believe that this hypo-immunity is largely due to a reduction in phagocytic functions. In contrast with this general agreement the effect of similar nutritional deficiencies on *antiviral* resistance is still controversial. At present there

are affected in addition to the diaphragm, respiratory failure and death ensue. Intercostal paralysis is recognized by failure of the thorax to expand and by retraction of the lower ribs during inspiration.

Involvement of the muscles which aid in support of the spinal column usually is not detectable until some time after the acute stages of the disease have passed and severe spinal deformities develop

The affected extremities are cold, mottled with a purplish blue color, and slightly swollen.

The brain-stem type of poliomyelitis selects the motor nuclei of the cranial nerves. As a rule, however, the cranial nerve paralyses do not persist. Third and fourth nerve paralyses are common The fifth and the twelfth nerves are usually spared. The facial nerve is usually spared The sixth nerve is the one commonly affected in ocular palsy Paralysis or weakness of the soft palate, the pharynx, and the vocal cords, and irregularities of pulse and respiration are present in tenth nerve involvement The voice is hoarse and swallowing is difficult

There is leukocytosis, the concentration of leukocytes ranging from 15,000 to 30,000 per cubic millimeter of blood, beginning in the prodromal stage and persisting for 6 or more weeks The lymphocytes may be diminished, and thus occasionally the total leukocyte count is normal owing to this reduction of lymphocytes and increase in other white cells

During the first week the cell count of the spinal fluid is often between 50 and 100 or more per cubic millimeter. Lymphocytes predominate in the spinal fluid throughout the course of the illness. In 2 weeks the cell count returns to normal values The globulin content during the first week is normal Thereafter, its value increases and the increase may persist for several weeks to more than a month The content of sugar and chloride is within normal limits.

The spinal fluid is never purulent and yellowish in poliomyelitis. The only time that there is an increased polymorphonuclear leukocyte count in poliomyelitis is during the early stages of the disease, prior to the time when paralysis is present. If the cells are predominantly leukocytes, the probabilities are that bacteria cause the condition, and they can be identified on a stained smear

When there are mixed types of cells and the proportion of lymphocytes is greater than that of leukocytes, either the patient is recovering from an acute infection which might have been pyogenic in origin, commonly an irritation of the meninges, or some disease is developing which ordinarily causes a lymphocytic reaction A second puncture to determine the further progress of the disease is indicated If the ratio becomes more lymphocytic, it is recognized that probably the disease is one causing lymphocytic reaction If the cells are predominantly lymphocytes, it is known that the disease is an encephalitis of some character

The amount of protein present in the spinal fluid gives a clue to the severity of the involvement

Diagnosis The presence of fever, signs of meningeal irritation, flaccid palsies and the changes in the spinal fluid are diagnostically definite.

During the summer any patient from 3 to 10 years of age who has difficulty in speaking, difficulty in clearly enunciating syllables, sounds, words, and especially consonants, or who has any difficulty in swallowing solid foods or liquids, should be s

stag

the disease may be suspected or diagnosed, but when this form occurs sporadically, it cannot be diagnosed.

In influenza there may be a stiff neck, and the gastrointestinal symptoms may be the same as those in early poliomyelitis However, the neurologic and spinal fluid findings are negative

knees, hips and back are forced to become deformed. Paralysis of the intercostal muscles may permit gross deformities of the thorax.

The unaffected muscles eventually undergo contracture. The paralyzed muscles are placed under tension which exerts an injurious effect on them As the result of excessive fatigue and strain, weak muscles may become paralyzed long after the active disease has ceased. In limbs with muscles paralyzed sufficiently to inhibit their use, the bones fail to grow and they undergo decalcification, causing an increased excretion of the calcium in the urine.

EXAMINATION On physical examination it may be observed that the patient lies quietly in bed and does not wish to be disturbed There are irritability and resentment against being moved or handled. The painful sensitivity of the peripheral tissues indicates the presence of spasm, a common and useful observation. Stiff neck, stiff back and shortened hamstrings are familiar examples of symptoms caused by the disease, but muscles elsewhere in the body may also be involved by spasm The muscular tenderness occurs in the nonparalytic as well as the paralytic individuals.

When the examiner places the hand beneath the patient's head and attempts to flex the neck, resistance will almost invariably be encountered as early as clinical symptoms have become manifested. An attempt to flex the body will disclose stiffness of the back When the trunk is flexed, the knees will rise from the bed because of shortness of the hamstring muscles. The stiffness is due to the condition of spasm in the posterior muscles On search, the same hypertonicity and shortening may be found, although less frequently, in other muscles of the body and in all types of cases

The patient may complain of pain in the muscles involved by spasm, or pain may be elicited by gently stretching the affected muscles. Involvement of the muscles of any part of the respiratory mechanism hampers the breathing. Spasm may affect the abdominal muscles.

Spasm occurs more frequently in the paralytic than in the nonparalytic patient. The value of this observation for the purpose of diagnosis is diminished by the fact that paralysis is not a common early condition and may not occur at all Paralysis occurs at some time within 15 days of onset in two thirds of the cases Neither weakness nor paralysis appears as an initial symptom, as a rule, and in only a few cases does this condition develop during the first 24 hours.

Patients who have bulbar symptoms, such as difficulty in swallowing, nasal regurgitation, facial weakness, and difficulty in speech, reveal muscular dysfunction, on the average, slightly earlier than patients in whom the spinal type of paralysis develops

It may be observed that there are twitchings in certain muscles and that in these same segments there is an increase of tendon reflexes accompanied by pain and tenderness. In some muscles the reflexes are diminished or lost and weakness and paralysis are present. The paralysis may be found on the first, second or third day of the illness but it may be delayed until the seventh or eighth day The paralysis may begin in the legs and ascend to involve groups of muscles higher up. It may be observed that the paralysis, after remaining stationary for several days or weeks, has extended once more In the early stages of the disease, ankle clonus or even plantar extension may be found

In the leg the quadriceps femoris, the peroneals, the flexors of the foot and the extensors of the toes are more commonly involved than other muscles The iliopsoas and the gluteals are often selected In the upper extremity the deltoid, the spinati, the flexors of the elbow and the supinators of the forearm are often involved Paralysis of the muscles about the shoulder joint and upper arm is common.

The diaphragm is usually affected in association with paralyses of the arms and the muscles of the shoulder girdle. In cases of diaphragmatic paralysis, breathing is thoracic with the epigastrium retracted during inspiration. If the intercostal muscles

tion with poliomyelitis and has some characteristics in common with that disease. These viruses differ immunologically from poliomyelitis viruses and do not cause the lesions of poliomyelitis when injected into monkeys The role of the newly discovered viruses in the causation of human disease is still uncertain

Tetanus (*Lockjaw*). In contrast to degenerative or destructive lesions of neuromuscular apparatus involving the muscles, as in the dystrophies, or the nerves primarily or the cells of the spinal cord, as in acute anterior poliomyelitis, is the hyperirritability of muscles in tetanus or lockjaw However, the very early manifestation of both of these diseases is muscular spasm.

As a rule, *Clostridium tetani* does not multiply within the tissues except in the presence of necrotic material Thus puncture wounds and buried splinters offer favorable conditions for a focus of this infection The organisms do not reach the nervous system The toxin reaches the nervous system by extending inward along the nerve trunks Once within the central nervous system, the toxin diffuses rapidly However, according to Abel, the toxic conditions caused by tetanus are created by three processes: (1) a local lymph-borne intoxication of the muscles or motor nerve endings, (2) a generalized effect of the same nature due to blood-borne toxin and (3) a series of symptoms due to the action of the blood-borne toxin on the anterior horn cells of the spinal cord (see Chapter 18).

The *incubation period* of tetanus averages about 7 to 8 days but may be prolonged to several weeks or even months in cases in which antitoxin has been administered. One attack does not necessarily bestow immunity

Symptoms. The first characteristic symptom of tetanus is tightness and twitching of the muscles There is trismus of the muscles of mastication The posterior cervical and abdominal muscles are affected early.

In the localized forms of the disease the first symptom is a constant spasm of the muscles in the neighborhood of the wound The spasm extends and frequently involves a whole limb. The symptoms may gradually advance for a week or two and the intense muscular spasm then may persist for two months. Local tetanus is less serious than the general form

Tetanus infections of the face, neck or head may produce a cephalic type of tetanus It begins with spasm of the facial muscles on one or both sides or with involvement of the jaws or pharynx Cephalic tetanus may remain localized or may be followed by a generalized tetanus In a few favorable cases the spasms grow less frequent and severe and the rigidity diminishes in a few days The trismus is often the last sign to disappear Convalescence is slow When the disease is fatal, death occurs in 3 or 4 days In some cases of fulminating tetanus death may result from asphyxia within a few hours The temperature often remains normal until toward the end The development of high fever is a bad prognostic sign

Examination On repeated examinations the tightness of the muscles is observed to increase. Pressure over the affected muscles and efforts to stretch them cause severe pain As the disease progresses, it is observed that the muscular movements grow more and more limited, and finally it is observed that constant and intense contracture of the muscles has developed so that the muscles have become immobile with spasm The spasm progresses successively to the muscles of the spinal column, the abdomen, the thorax and the legs, and to the arms When all the muscles are involved with spasm, the legs are extended, the head is retracted and the trunk is arched backward into a position of opisthotonos The arms are flexed and the fingers clenched The angles of the mouth are retracted (risus sardonicus), the eyelids partially closed, and the eyebrows elevated. By this time the bulbar muscles are affected and dysphagia, aphonia and cyanosis are present.

Owing to sphincteral involvement there is retention of urine and feces. The [illegible] f respiration

[illegible] ecome more frequent and more prolonged The pain is horrifying to the patient, and its apparent

The patient who has rheumatic fever may not be able to move the legs because of pain; the immobilization, however, is voluntary. There are present pain at the insertion of the tendons or in the joints involved, perhaps a cardiac murmur, and a good therapeutic response to salicylic acid.

In postvaccinal encephalitis there are present encephalitic irritability followed by stupor, a history of vaccination, and a relatively low lymphocyte count with an extremely high protein content in the spinal fluid. If the patient is seen at the onset, there are signs of an upper, but not of a lower, motor neuron lesion. Later, during coma, neurologic reactions may be absent.

In lymphocytic choriomeningitis (acute benign idiopathic meningitis, acute aseptic meningitis, benign aseptic choriomeningitis, epidemic meningitis serosa, or serous meningitis), the onset is acute and the progress rapid, and it occurs in any age group at any time and in any locality It is accompanied by headache, muscular pains and sometimes constipation. Neither muscle weaknesses nor neurologic signs are present, except perhaps in a positive Kernig sign and a stiff neck Examination of the spinal fluid reveals normal sugar and chloride, negative reactions to all tests, a meningitic gold curve, a cell count ranging from 20 to more than 1,000 cells per cubic millimeter, 90 per cent of which are lymphocytes, with little or no protein It is therefore evident that it is impossible to separate this disease from an abortive type of poliomyelitis when it occurs during an epidemic of poliomyelitis

The spinal fluid in equine encephalomyelitis usually is clear to ground-glass in appearance and contains from 200 to 2,000 cells per cubic millimeter, mostly polymorphonuclear leukocytes, the globulin is 4 plus.

Tuberculous meningitis in its inception is difficult to differentiate from poliomyelitis. Time may be required for the differentiation A patient who has tuberculous meningitis remains ill for days, with but few symptoms and little or no fever and with no paralysis of muscles. Specific organisms are present in the spinal fluid.

The Coxsackie Viruses. Investigation of small epidemics of poliomyelitis led to the isolation by Dalldorf and Sickles, from fecal specimens of 2 children in the acute phase, of an agent that induces paralysis in suckling mice and hamsters. This paralysis is associated with destructive lesions of skeletal muscles, the central nervous system being unaffected.

Howitt reported isolations of the Coxsackie group of viruses from the secretions or tissues of patients from Alabama, Colorado, Delaware, Florida, Georgia, Louisiana, Oklahoma, South Dakota and Tennessee

The Coxsackie virus may be isolated from human feces, urine, nasopharyngeal or oral washings, oral vesicles, nasal swabs, saliva, sputum, serum, whole blood, cord and brain. The virus has been isolated in sporadic cases and from groups of patients who had variable and ill-defined symptoms such as mild fevers, poliomyelitis-like or influenzal syndromes and occasionally encephalitis

Howitt's study revealed Coxsackie virus in the tissues and secretions of 10 patients whose disease was fatal, in 5 of 10 cases the diagnosis was poliomyelitis. Poliomyelitis virus was recovered also from the spinal cord of 1 of these patients and from the feces of 2 patients who had recovered. Howitt and Benefield were able to differentiate the Coxsackie virus into serologically distinct types by the complement fixation test with filtered muscle antigen. The same test can be employed for determination of the presence of antibodies in human serums. At least two immunologic types of the virus exist The virus has been isolated from the sewage of a number of cities and from flies collected in widely separated areas

Findlay has cited evidence to suggest that Coxsackie viruses 1 and 2 are widely distributed in Great Britain and that some epidemics of Bornholm disease (epidemic pleurodynia) in that country are associated with infection by Coxsackie virus 1 or 2 or closely allied viruses. It is, therefore, apparent that there exists a common infectious disease caused by the Coxsackie virus group that occurs in close associa-

more there may remain a detectable defect in conjugate deviation of the eyes toward the paralyzed side.

The upper part of the face is but slightly weakened. The facial weakness is more evident on voluntary than on emotional movement. At first it may be impossible to wink the eye of the affected side without closing the opposite eye. Voluntary movement is most severely restricted or abolished in the arm. Both the arm and the leg reveal the hypertonicity and reflexes characteristic of an upper motor neuron lesion. There is weakness of trunk muscles revealed by the inability of the patient to sit up in bed and often to turn in bed There is a tendency to fall toward the paralyzed side when standing is permitted or attempted

The affected arm slowly adopts an attitude of general flexion and adduction. The leg develops an attitude of extension and outward rotation. The foot is plantar flexed, and it so remains. The demented hemiplegic patient tends to lie on the contralateral side, which permits flexion of the ipsilateral leg Flexion of both legs ensues because of disuse too of the contralateral leg This attitude of flexed legs becomes fixed unless prevented by braces The addition of braces makes it very difficult to give nursing care

On examination when the hemiplegia has become fully established, the findings are those of the upper motor neuron lesion Isolated movements of the fingers and all skilled movements of the hand, extension of wrist and fingers, extension at the elbow, clenching of the fist, and flexion at the elbow are affected Elevation and adduction at the shoulder are but slightly impaired Dorsiflexion of toes and foot, eversion of the foot, flexion at knee and hip, plantar flexion of foot and toes, and, least severely, extension at knee and hip and inversion of the foot are reduced or abolished.

The movements of the lower part of the face are more severely impaired than those of the upper part. Deglutition is unaffected, but articulation may be transiently or permanently disordered.

The increase in muscular tone is more evident in the musculature of the arms and legs. The increased tone, or spasticity, however, is variable in the muscle groups For instance, in the upper limbs it is most marked in the flexor muscles of forearm and arm and in the adductors of the shoulder In the lower limbs it is characteristically most marked in plantar flexor and extensor muscles Its presence is detected by passive stretching of the muscles and observing an increased resistance. An increased resistance is easily elicited in the knee extensors While the patient is reclining in bed, request him to rest the thigh upon the examiner's forearm; the examiner's other hand grasps the leg just above the ankle and flexes the leg at the knee Slight flexion is normally permitted without marked resistance. However, as flexion is increased, an active resistance develops quickly in the quadriceps muscle, and more force is needed to continue the flexion After the knee is flexed to approximately 45 degrees, the resistance ceases and the rest of the movement is carried out normally In spastic paraplegia it may be difficult to flex the leg passively In instances of mild hemiplegia only mild muscular hypertonus may be appreciable in the flexors of the fingers and in the plantar flexors of the foot

The loss of cutaneous reflexes is not an invariable feature of upper motor neuron lesions. The extensor (Babinski) type of plantar response is present in an upper motor neuron lesion. This reflex may be obtained from both cutaneous and deep stimulation Pinching the skin of the foot or leg, pressure over bony points around the ankle, or a stroking pressure over the shin, may elicit the response. Thus Oppenheim's, Gordon's and Chaddock's reflexes are not more than the extensor plantar response elicited from different parts of its wide receptive field The extensor type of plantar response in those who have paraplegia-in-extension may be accompanied by plantar flexion of the foot and great toe of the opposite side, the so-called crossed plantar response

intensity defies description, for the patient does not lose consciousness. The spasm may be so great that fractures of the vertebrae ensue. A moderate leukocytosis is present. The spinal fluid is normal. The pressure is increased.

DIAGNOSIS. The history of a wound, the trismus, the opisthotonos, risus sardonicus and abdominal rigidity and the tonic muscular spasm persisting between the paroxysms are diagnostic.

There is a mortality rate of less than 50 per cent if patients are properly treated with antitoxins.

In treatment for tetanus an antitoxin is used The American unit of antitoxin is defined as 10 times the least amount of serum necessary to save the life of a guinea pig weighing 350 gm for 96 hours against the standard test dose of toxin The standard dose of toxin is 100 M L D of a standard toxin preserved at the National Institute of Health.

The Upper Motor (Pyramidal) Neurons and Locomotion. It has been indicated in the preliminary definitions that upper motor neurons, at least a few of them, arise from the Betz cells of the cortex and pass uninterruptedly to the anterior horn cells of the cord It is for the purpose of definition that these neurons have been singled out, for in reality the pyramidal system is a twofold communicating system. It is an internuncial path interposed between the distance receptors and their central cortical connections, and the motor mechanisms of the nervous system. Through the pyramidal system pass all the impulses which instigate willed movements of skeletal muscles. These movements are activated and designed by the cortical (frontal lobe) afferent patterns of excitation

As the complexities of the nervous system prevail, it must be added that in the manifestations of the lesion of the upper motor neurons there are evidences also of overaction in subordinate extrapyramidal neurons. This overaction of the extrapyramidal neurons is manifested by spasticity, increased tendon reflexes, clonus, and the extensor type of plantar response These reflex changes have their origin as the result of a loss of influence of the pyramidal neuron The symptoms are often designated release symptoms

Hemiplegia. Hemiplegia represents a common acute or chronic manifestation of an upper motor neuron lesion. Hemiplegia is caused by a lesion of the brain on the side opposite (contralateral side) the paralyzed muscles of the face, arm and leg. Usually developing acutely, it passes through an acute phase and then subsides, leaving the muscles hypertonic or spastic—the spastic phase Initially the onset is sudden and the patient is found unconscious, lying with the head and eyes turned away from the side of the lesion Often there is a slight ptosis of the eyelid on the affected side. The cheek on the paralyzed half of the face flaps in and out with each breath. If the breathing is stertorous, the increased amount of sputum is spattered over the face, clothing or bedding. The entire musculature is flaccid The flaccidity of the affected side of the mouth and the thigh is most noticeable. The paralyzed thigh muscles spread out as the patient lies supine and give this part of the limb a broader appearance than the other one. The tongue may be thrust out toward the hemiplegic side. It is impelled outward by the genioglossus muscle of the normal side. The tongue returns to the mouth within an hour or two except in those patients who remain severely paralyzed The base of the tongue often remains higher on the paralyzed side than on the opposite side

For a week or more the temperature of the hemiplegic half of the body may be from 1.5 to 2 F higher than of the opposite half. Often acute trophic lesions develop: edema of hand and foot with blistering, and bedsores The abdominal reflexes are abolished on the paralyzed side. Only in the most deeply comatose patients are the tendon jerks abolished. The plantar response is extensor on the affected foot The shock usually passes off after a few hours and the patient regains consciousness, and on restoration of consciousness release symptoms appear. The deviation of the head and eyes away from the side of the hemiplegia passes off, but for a week or

be local invasion from osteomyelitis of the vertebrae or from furunculosis with an ensuing septicemia. Purulent myelitis and even abscess of the spinal cord may occur in various types of septicemia, but these are rare

Tuberculous spondylitis may cause sudden paraplegia although, as a rule, the onset is slow.

Acute spastic paraplegias in association with other types of infection such as those due to the viruses of measles, vaccinia, varicella or mumps may appear without any other evidence of involvement of the nervous system An acute paraplegia may follow a febrile illness of obscure nature or may occur without apparent cause.

Paraplegias-in-extension due to pyramidal (upper motor neuron) lesions in the cord develop slowly. The toe begins to drag and it is frequently stubbed The sole of the toe of the shoe is worn on the inner side This difficulty in locomotion is enhanced by the flexion weakness of the leg, and shuffling gait ensues Spasticity develops in the extensor and plantar flexor muscles The plantar response often is extensor in type. The legs come to be rigidly extended and abducted Paroxysms of spontaneous clonus or sudden single extension spasms are experienced

Paraplegia-in-flexion occurs when there is a more complete interruption of conduction of descending impulses in the cord than is present in paraplegia-in-extension

Involuntary flexor spasms increase, and finally the legs come to lie flexed, with the knees pressed against the abdominal wall If the legs are forcefully extended they rapidly resume flexion The extensor type of plantar response may be obtained from the middle of the thigh, downward by pinching or pricking the skin, or deep stroking over bones and muscles The knee jerks, and later the ankle jerks, may diminish and become difficult if not impossible to obtain

The diagnosis is established by the history and the physical findings Identification of the organism by bacteriologic culture is helpful in treatment.

Injuries of the spinal column may involve the spinal cord as a result of hemorrhage or compression by dislocation of intervertebral disks or the vertebrae themselves Often, in instances in which the injury of the cord is due to trauma, dislocation of the intervertebral disks or fracture of vertebrae may not be demonstrable on roentgenologic examination Such lack of evidence of injury is explained by the fact that dislocations of the vertebrae are reduced spontaneously In rare instances dislocation of a vertebra (the first or second cervical) has occurred spontaneously, and such an occurrence may cause paraplegia or may cause sudden death

During the course of *multiple sclerosis,* especially in association with an optic neuritis from the same cause (neuromyelitis optica), a spastic paraplegia may occur In these cases the paraplegia may improve

The diagnosis depends on the association of acute transverse myelitis, optic neuritis, and other symptoms of multiple sclerosis

Paraplegias of gradual onset may be due to *extradural sarcomas and gliomas,* fibromatous tumors of Recklinghausen's disease, syringomyelia, tuberculous spondylitis, and severe kyphosis of nontuberculous origin

The diagnosis of these conditions depends on expert interpretation of myelograms made with experienced hands

Extrapyramidal Neurons and Locomotion. It has been stated that the extrapyramidal tract consists of short neurons intercommunicating with parts of the pyramidal system (upper motor neurons) and that this system is presided over in some degree by the pyramidal system These short tracts connect with the corpus striatum, the substantia nigra, corpus subthalamicum, red nucleus, vestibular and reticular nuclei, and long descending tracts, the rubrospinal, vestibulospinal and reticulospinal

The essential clinical components of the different syndromes of extrapyramidal

When the hemiplegic patient yawns or stretches, as during any forceful or sustained movement of the normal limb, the affected arm tends to extend at the elbow, wrist and fingers, remaining rigidly in this new attitude until the yawn passes off. Simultaneously the leg goes into rigid extension with the foot plantar flexed. These phenomena are not associated movements, but rather are phenomena in the normal maintenance of posture.

Due to the fact that the arm and hand have been freed of locomotor functions, their movements are controlled from the cortex and are therefore largely acquired or learned movements The degree of loss of movement is permanent. The hand rarely regains any movements other than simple flexion of all the fingers simultaneously and simple movements of flexion and extension at the wrist. The movements of the face and leg are more primitively spontaneous and natural and thus more recovery will take place in them than in those of the arm and hand The extensor (Babinski) plantar response on the paralyzed side, however, remains freely elicitable Hemianesthesia, with or without a crossed homonymous hemianopsia, may accompany the hemiplegia. This occurs only when the posterior limb of the internal capsule is extensively destroyed, the sensory radiations which lie caudal to the pyramidal fibers, and the optic radiations which are placed still further caudally, are affected

There is an upper and a lower motor neuron type of paralysis of ocular movements In paralysis of the upper motor neuron there is a loss of co-ordinated movements. In paralysis of the lower motor neuron there are characteristically present diplopia and squint unless there is complete external ophthalmoplegia The upper motor neuron type of paralysis is a supranuclear paralysis of which there are two varieties. one when the voluntary initiation of conjugate movements is lost, but such movements can still be evoked by reflex stimulation; the other when such movements are totally lost and cannot be elicited In total blindness resulting from bilateral destruction of the visual cortex, the pupillary reactions may remain intact. The lower motor neuron type of ocular paralysis does not occur in hemiplegia

Paraplegia. Paraplegia is a paralysis of the lower part of the body and the legs caused by disease or injury of the upper motor neuron in the spinal cord Both motion and sensation are affected Paraplegia may exist in extension or in flexion.

Common causes of paraplegia are defective development of the spinal cord, infections, injury to the spinal cord, locomotor ataxia, transverse myelitis, chronic alcoholism, malaria, and pernicious anemia

Defective development of the spinal cord, or myelodysplasia with spina bifida, as has been stated in relation to lower motor neuron lesions, usually causes flaccid paralysis and atrophy of the legs. Rarely will a defect in the cervical segments of the cord produce spastic paralyzed legs with knee jerks increased Frequently in the presence of spastic paraplegia there is some atrophy of the muscles of the hands and forearms and, perhaps, loss of pain and temperature sensibility as in syringomyelia.

The diagnosis of these congenital lesions of the pyramidal tract with spastic paralysis is made by physical examination and by the finding of an area of defective cutaneous development overlying defective vertebrae, demonstrated by roentgenologic examination.

In some instances vascular anomalies such as congenital arteriovenous fistulas or venous angiomas may cause sudden spinal paralysis from pressure or rupture. Occlusion of the abdominal aorta at the bifurcation may cause anemia of the cord and sometimes paraplegia.

Pyogenic infections, having produced a pyemia, may originate an infection of the epidural space causing either a granulomatous process with compression of the cord or an extensive purulent process with a rapidiy ascending paralysis which is almost always rapidly fatal The other causes for infectious spastic pa[illegible] may

are accompanied by great excitement and often delirium These movements fulfill the requirements for an extrapyramidal origin arising in the short extrapyramidal neurons in the cortex.

The Cerebellum and Locomotion. The cerebellum functions with the pyramidal system in the maintenance of posture. The harmonious control of the combination of movement and posture is a function of the cerebellum When there is a loss of function of the cerebellum, voluntary movement is grossly disordered and cerebellar ataxia ensues.

Cerebellar Ataxia. Cerebellar ataxia according to Walshe is a disturbance of postural fixation. In acute cerebellar ataxia there are flaccidity and atonicity of the muscles. In chronic cerebellar ataxia there is fixation of the parts while actually in movement as well as of the parts which should be maintaining attitude in the rest of the musculature. The true expression of a cerebellar ataxia is a defect in tone of the muscles. This tonal defect is expressed by abnormalities in the movements of the eyes, of the muscles of articulation, and of the hands, arms and legs.

The ocular movements are manifest on conjugate deviation to the side There is a series of regular horizontal jerks, nystagmus The eyes can move normally laterally. The abnormality is evidenced by inability to sustain the lateral deviation The eyes drift slowly toward the midposition During the slow movement of the eyeballs back to midposition they are suddenly jerked back to the deviated position In unilateral cerebellar abscess and auditory nerve tumors, the nystagmus is slower and its range wider when the eyes are moved toward the side of the lesion than when they are turned away from the side of the lesion

The movements of the muscles of articulation are so affected as to produce scanning speech In scanning speech each syllable is pronounced deliberately and slowly. Movement of the hands reveals an intention tremor, irregular in rate and amplitude and excessive in range

The abnormality of the movement of the hands and arms is easily demonstrated by having the patient touch the index finger tip to the nose The hand and arm commence their course normally but soon an irregular course begins with a to-and-fro jerky movement which increases in width as the finger approaches its destination. The finger finally punches or misses the nose and for an instant continues to wiggle about the end of the nose All movements of the hands are likely to be forceful and to overshoot the mark.

Because of irregular swaying of the body, the gait is irregular and staggering and the maintenance of stance difficult It seems that the arms and legs are not ready to stop on command Sensations are undisturbed The tendon jerks are exaggerated In unilateral lesions the postural disturbances are limited to the side of the lesion

[illegible]

becomes evident in the first two years of life. There is ataxia, with intention tremor of the arms and unsteady gait of cerebellar type. The symptoms remain unchanged throughout life

ACUTE ATAXIA Acute cerebellar ataxia may occur as the only manifestation of encephalomyelitis due to measles, varicella and other acute infectious diseases. Cerebellar ataxia may occur in association with any widespread lesions in the nervous system. Cerebellar abscess is a cause of acute cerebellar ataxia. There are usually present, of course, otitis and mastoiditis, as well as fever, leukocytosis and intracranial hypertension

Cerebellar Deficits. In the syndrome of generalized cerebellar deficit there is [illegible] is im- [illegible] This [illegible] from [illegible]

disease of the motor system are disorders of muscle tone and involuntary movements. Walshe has described these as three main symptom complexes: (1) the syndrome of paralysis agitans (tremor-like rigidity), (2) athetosis and (3) the choreiform syndrome.

Paralysis Agitans (Tremor-like Rigidity). In paralysis agitans according to Walshe there is a uniform muscular hypertonus throughout the entire range of passive or active movement of all muscles except external muscles of the eye. On palpation the muscle has an increased tonus which yields only when an appropriate force is applied On forcefully stretching such a muscle, as on extension at the elbow, there is a jerky relaxation simulating the lowering of a lever by a cogwheel, thus the term cogwheel rigidity This rigidity slows the speed and the range of movement so that facial expresion lessens and finally disappears, giving the patient a masklike rigidity of expression Excessive emotional stimuli are required to break up this rigidity When the patient smiles, the smile moves slowly over the face, and once it has spread, it remains too long In walking, the arms cease to swing and the legs move slowly and in short steps (loss of associated movements). There is a tremor which is a rhythmic movement In mild extrapyramidal involvement the tremor ceases when the patient is at rest, and even in severe instances of involvement it ceases while the patient is asleep Occasionally it may cease while the limb is in active use. During stresses of emotion or in fatigue the tremor increases The tendon jerks are increased, but clonus is absent The plantar response is flexion Occasionally the tremor is entirely absent throughout the course of the illness.

The common form of paralysis agitans or Parkinson's disease affects aging individuals as a part of the manifestations of arteriosclerosis. Less commonly, in its most highly developed form, the disorder is a manifestation of chronic encephalitis, subsequent to an acute encephalitis, a viral disease which occurs sporadically, endemically and epidemically (Von Economo's encephalitis). (See Chapter 15.)

Often the disease begins with aching in the arms, to be followed by tremors of the fingers The tremors may be limited for months to a hand or a foot In due time there is a manifest hypertonia of the muscles more definitely expressed in the flexors than in the extensors As soon as hypertonia is established, the head and body become bent forward, and there is, as well, a slight flexion everywhere in all of the muscles The gait is slow and shuffling and often the patients complain of propulsion or retropulsion The voice is high-pitched, weak and monotonous There is difficulty in beginning to speak, but once started the words are uttered rapidly.

Many and varied are paresthesias and aching pains Disturbances in sweating are common The face is often flushed and expressionless or masklike

The tremor advances, until it finally is slowed after the patient is confined to bed Utter helplessness is often present just prior to death.

Athetosis. The variations in the muscular hypertonus of extrapyramidal lesions seem in some instances to be the cause of slow twisting movements and distorted postures of the arms and legs with fingers hyperextended These movements are aggravated in force and amplitude when movement is performed when the patient is hurried or emotionally tense. No signs of upper motor neuron lesion may be found except in those who have in addition an infantile hemiplegia The movements of the face, tongue and articulation are not affected except in rare forms of bilateral athetosis.

The Choreiform Syndrome. In contrast to the movements of paralysis agitans and athetosis, choreiform movements are associated with diminished muscular tone. These movements are superimposed upon voluntary movements. They are jerky co-ordinate movements of the limbs, trunk and facial muscles The involuntary movements of rheumatic chorea are not associated with extrapyramidal disorders and therefore are described elsewhere in this text (Chapter 18). In severe chorea such as chorea gravidarum, the movements are incessant, of great violence, a

vidual has good vision and is able to see written words but does not understand them, the condition is termed *word blindness* If an individual does not comprehend spoken words there is a *sensory aphasia* If there is only injury to a motor eupraxic center the speech musculature is incapable of forming words, though all other movements in which it functions are normally performed, the condition is *motor aphasia.* When writing movements cannot be made there is *agraphia* A failure to recognize the nature or use of a familiar object such as a spoon is *agnosia.* An individual who has neither paralysis, ataxia of movement, nor sensory loss, yet cannot perform the movements appropriate to the use of a familiar object, has *motor apraxia*

Sensory aphasia consists in an impaired or lost comprehension of the spoken word: expression through speech is disordered It is postulated that the eupraxic center transmits the wrong speech patterns to the motor cortex, and thus wrong words are uttered. These words are often badly arranged, and the patient, being word deaf, is unaware of the mistakes One affected with word deafness cannot carry out spoken orders.

Motor aphasia in its mildest form consists in a loss of memory for the names of familiar objects. In more severe degrees of aphasia the patient is reduced to the utterance of a single word such as "Yes," or perhaps "Yes, yes " (See Diseases of the Larynx, Chapter 4)

In aphasic subjects there is a tendency, when some other movement is asked for, to repeat a movement that already has been carried out to order.

Agnosia and *apraxia* are detected by giving the individual familiar objects and thus determining the capacity to recognize their nature and use. *Motor apraxia* is detected by the presence of an inability to perform familiar but simple movements

THE SENSORY SYSTEM AND LOCOMOTION

All acts of locomotion are initiated by the sensory nervous system. The organs of sense, namely, the eyes, ears, nose, taste buds, touch spots in the skin, and the nerve beginnings in the muscles, bones, joints and viscera, are so constructed as to analyze the environmental energy and select certain kinds of disturbances which are then transformed in the receptor and give rise to nervous impulses These nervous impulses on arrival in the appropriate area in the brain originate visual, auditory, and olfactory sensations, taste, dermal sensation, positional sense of an extremity, or pain Aberrations or false interpretations of these sensations by the brain have been considered in association with the complaint Likewise, since pain is the commonest subject of complaint, the sensory perception of pain was differentiated from the reaction to pain All fibers carrying all of the sensations from the various end-organs in the skin and deeper skeletal tissues arrive at the dorsal root entry zone of the spinal cord Here the modes of sensation are grouped or integrated according to quality. Some impulses probably go no higher than segmented levels of the cord. The impulses for tactile, pressure, postural and vibratory sensibility course up the dorsal columns forming the uncrossed sensory paths ending in the dorsal column nuclei of the medulla Then secondary neurons, carrying the impulses through the decussation to extend upward, traverse the pons and the midbrain and end in the lateral nucleus of the thalamus In the lateral thalamic nucleus all sensations are again integrated, and from this nucleus the third and last neuron carries the remaining impulses which were not integrated in the thalamus to the sensory cerebral cortex and to consciousness

The superficial and deep impulses for painful and thermal sensations on reaching the cord enter the gray matter of the dorsal horn to join a secondary neuron which crosses the cord to reach the lateral column of the opposite side where it turns upward Painful and thermal sensations thus result from nervous impulses that follow crossed sensory paths (spinothalamic tract). Tactile sensibility too has

generalized cerebellar damage The chief differential diagnosis is from the spinal ataxias.

Cerebellar catalepsy and the rare cases of cerebellar fits, tonic in type, often with opisthotonos, are indicative of disease of the subcortical cerebellar nuclei.

In vertigo of cerebellar origin the surrounding objects appear as if rotating toward the side opposite to the lesion. However, this vertigo may be due to affection of the adjacent vestibular nuclei or their connections Likewise the upward and backward and lateral positions of the head are probably due to vestibular disturbances and not to primary cerebellar disease Implication of the vestibular fibers produces vertigo and spontaneous nystagmus laterally and vertically, together with impairment of thermic nystagmus and of other vestibular reactions on the affected side Occipitofrontal headache appears Later a vestibular attitude of the head may develop and there are signs of cerebellar compressions consisting of a reeling gait with a tendency to fall toward the side of the lesion. As the tumor enlarges, other cranial nerve palsies develop A facial nerve palsy is a sign of great localizing value when present

There may be subjective tingling or neuralgic pains in the distribution of the trigeminal nerve. Paralytic changes of the trigeminal nerve are evidenced by decrease or loss of sensation in the trigeminal area and loss of the corneal reflex on the side of the lesion Glossopharyngeal paresis and affection of the upper roots of the vagus produce unilateral palatal palsy on the side of the lesion.

The diagnosis of cerebellar disease is established by the presence of a cerebellar ataxia. If the ataxia is due to a degenerative disease, signs of intracranial hypertension are not present If the ataxia is due to an expanding lesion, such as a tuberculoma or a neoplasm, then papilledema, headache and vomiting are present If the tumor is situated in the posterior fascia of the cranium, there are evidences of involvement of the cranial nerves or there is pressure on the brain stem

In the absence of intracranial hypertension a differential diagnosis includes the possibility of the presence of multiple sclerosis, cerebellar encephalitis from any cause, and also lesions of the contralateral frontal and the contralateral parietal lobes of the hemispheres of the brain.

The Frontal Cortex and Locomotion. The disturbed functions of the frontal cortex which affect locomotion are termed eupraxic. Eupraxia is inexactness of the reproduction of known co-ordinated movements. It is the frontal cortex that stores the patterns for the skilled movements and movement-complexes, particularly of speech and the hand, that are learned during life The eupraxic centers cause the motor cortex to initiate voluntary motor activities when such are desired or necessary. Therefore a loss of function of the frontal cortex with its eupraxic centers causes, not a true paralysis of movement, but an inability to initiate movements at will All movements, however, may still be performed spontaneously when attention is not directed to their performance.

The Speech Function. Speaking and writing, physiologically, are movements; psychologically, they are symbols which express thoughts that refer to things

Disorders of articulation conform to the manifestations of upper and lower motor neuron lesions, the particular manifestation depending on whether the lesion is situated in the afferent (sensory) path, in the motor cortex, or in the efferent (motor) path. In cortical association areas articulated sounds heard, or written words seen, and the sensory impressions left by past speech movements are retained Any lesion cutting off the association areas from the projection areas, or a lesion within them isolating one part from another, will produce a true disorder of speech. The disorder may be sensory (receptive), motor (expressive), or a combination of sensory and motor defects.

If there is only a sensory defect, the hearing of word sounds is normal, but one so affected is unable to understand what is heard and has *word deafness*. If an indi-

The element of light contact or touch is tested by a camel's hair brush or a wisp of cotton touched lightly to the skin, the patient answering immediately on feeling the touch. Symmetric parts should be compared The power of localization is determined by touching the skin with the fingertip and asking the patient to close the eyes and put a finger on the same point. Any error greater than 2 inches is considered abnormal. Localization on the unaffected side should be tested.

For testing the temperature sense, test tubes containing hot and cold water may be used. Touch the surface first with one, then with the other, asking the patient in each case to state whether there is a feeling of hot or cold

A convenient way to test the weight sense is to use two coins differing in weight but preferably of nearly the same size Alternately and synchronously lay them on the extremity or part to be tested, and request the patient to indicate which is heavier. This sense is most acute on the brow, temples, forearm, dorsal surface of hand, and abdomen

The sense of position is tested while the patient's eyes are strictly closed or blindfolded. Taking hold of one of the extremities, flex, extend and move it in a variety of directions, asking the patient to imitate these motions with the corresponding limb of the opposite side, or place one limb in a certain posture and have him describe the position in which it remains

The power of co-ordination depends on the muscular sense, by which is ascertained the amount of strength to be employed, and on the articular and tendinous sense, which informs the sensorium of the position of the various limbs and parts of the body, for instance, the regular and smooth co-operation of individual muscles or muscle groups which are requisite to accomplish a definite action or movement. If these senses are dulled or abolished, the condition of *ataxia* exists However, in ataxia other factors are concerned such as sight and touch.

Ataxia is a disturbance of co-ordination of muscular movements, and is usually of three types. cortical, spinal and cerebellar In *cortical ataxia* the conduction fibers between different centers are usually involved, as in the speech defects of general paresis. In *spinal ataxia* the conducting fibers of deep sensibility are involved In *cerebellar ataxia* the sensory conduction fibers are involved, especially those of the vestibular apparatus In ataxias, eye control and disturbance of the sense of equilibrium and of vestibular control are the most important accompanying factors

Ataxia manifests itself in certain disturbances of station and gait or other voluntary movements. These disorders of co-ordination may be searched for as follows: Ataxia of the upper extremities is tested by having the patient close the eyes and touch, first with one index finger, then with the other, the tip of the nose, the lobe of the ear, the center of the closed eye, or the end of an indicated finger of the opposite hand, or, with the eyes open, to thread a needle, button the coat, or write If these attempts are successful, the co-ordination is good.

Ataxia of the lower extremities may be demonstrated by various methods Have the patient stand, eyes closed, with the heels and toes together. In a perfectly healthy person the swaying of the head will be very slight If ataxia is present, the swaying will be noticeable, and the patient, if not prevented, may even fall. This symptom is called static ataxia or the *Romberg sign* Ask the patient further to walk along a straight line Inability to follow the line signifies motor ataxia In instances of inability to walk, ask the patient, eyes open, to imitate with a foot the movements made by the examiner's hand, for instance, writing in the air, circles, or with eyes closed, to touch with the heel of one foot the knee of the opposite side (knee-heel test).

In all tests for ataxia which are made with the eyes closed, the patient should first rehearse once or twice the required movement with eyes open

In cerebellar and some cortical (frontal) ataxias the patient walks in a reeling, drunken manner, with short steps and feet wide apart. With eyes closed, the patient

a crossed sensory path (ventral spinothalamic tract) as well as traveling upward in uncrossed tracts.

All sensibility is divided into superficial and deep by Walshe, who recognizes four primary modes of superficial or cutaneous sensibility; namely, light touch, cold, warmth and pain. Likewise, deep sensibility is divided into four modes; namely, painless, painful pressure, postural sensibility and vibratory sense.

Each mode of cutaneous sensibility begins in the small groups of special end-organs and is conducted by its own conducting fibers. These special sense organs are at least doubly innervated by the dorsal root fibers so that when sense organs are sufficiently separated in space, two sensory stimuli can be felt and distinctly recognized (Walshe)

EXAMINATION. The superficial and the deep sensibilities may be tested by various means. The *superficial sensibilities* are conveniently tested as follows. (1) light touch, tested by cotton wool; (2) distinction of small differences between the points of a compass; (3) localization the patient indicates spot touched by examiner, (4) recognition of small variations (2 to 5 degrees) in the temperature of objects (a test tube of warm water), (5) pain sense, tested with a needle.

Deep sensibilities usually tested are those of muscular, articular and tendinous senses, as follows: (1) position, tested by imitating with the sound limb the position of the affected limb, by pointing with the sound limb; (2) passive movement: appreciation of movement, recognition of the direction of movements; (3) active movements: imitation of movement by the sound limb, (4) weight sense: (a) with hand supported, recognition of differences in weight; (b) with hand unsupported, comparisons of weight placed in each hand; (5) sensibility of bone, tested by a tuning fork of low pitch over bony areas; (6) joint sensibility, tested by flexing and extending joints, (7) temperature sense, tested by hot and cold test tubes.

These sensory functions are examined in order to determine whether they are abnormally active, absent or perverted In testing the cutaneous and pain senses, the patient's eyes should be kept strictly closed or blindfolded, and instructions given that the patient make prompt response at the instant the artificial stimulus is perceived, using always the same word, "Yes" or "No," but otherwise keeping silent. Promptness of response is important, for slowness in response may indicate a delay in conduction The time elapsing between stimulus and response is, under normal circumstances, one tenth of a second, in disease it may be 10 seconds. In testing tactile, temperature and pain sensibility, the areas in which disturbances are found should be outlined In some instances it is necessary to examine not only the cutaneous surface but also the mucous membrane of the nasal and oral cavities and the external genitalia. The following methods are useful

In order to determine the sensibility to small differences between points on the skin, ordinary compasses with their tips guarded by bits of adhesive plaster, a hairpin, or the heads of two ordinary pins, may be used The patient's eyes being closed, the points are placed on the skin sufficiently wide apart to be recognized as a double contact and gradually brought together until it appears to the subject that he is being touched with a single point only Note also whether one point is felt as two or more; and whether a touch on one side of a limb, or of the body, is felt respectively on the other side of the limb, or on the opposite side of the body The sensibility varies within wide limits. These limits are learned by the examiner through experience

The tip of the tongue is most sensitive; it can differentiate between points 1 mm (about 1/25 inch) apart The finger tips are the next most sensitive areas. In the following order the distance of point differentiation decreases: lips, dorsal surfaces of fingers, tip of nose, forearm, tips of toes, cheeks, eyelids, temples, backs of the hands, neck, leg, dorsa of feet, back, arm and thigh. Over the thigh the patient does well to differentiate points 3 to 4 inches apart

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in walking may reel first to one side or the other, or fall forward or backward. In the frontal, cortical ataxias, which closely resemble cerebellar ataxias, the symptom known as adiadochokinesia (inability to make certain rapid fine movements of the hands, such as five-finger exercises, or rapid wiggling of the toes) is usually absent. In cerebellar ataxias it is more often present

Anesthesia, according to a strict definition, indicates a loss of light touch sensibility, but the term is often employed to denote a loss of any form of sensation. The distribution of tactile anesthesia is somewhat varied. It may be either psychic or due to some organic lesion In general, the most important diseases or conditions which present anesthesia as a symptom are cerebral lesions causing hemiplegia; hysteria and traumatic neuroses, disease of the posterior column, roots, or horns of the spinal cord, especially locomotor ataxia; pressure on the cord (tumor, fracture); neuritis (a frequent cause), and leprosy.

Hemianesthesia is a loss of sensibility confined to one lateral half of the body. When found it is, in the majority of cases, a symptom of hysteria It usually affects the left side, and terminates very exactly at the middle line of the body Not infrequently there is anesthesia of the senses of hearing, taste, smell and sight on the same side The next commonest cause is a lesion of the posterior third of the posterior limb of the internal capsule, at which point the sensory fibers pass upward. Under such circumstances it is usually incomplete and is conjoined with hemiplegia of the same side. Hemianesthesia and hemiplegia on the same side plus oculomotor paralysis of the opposite side (crossed ocular paralysis) are indicative of a lesion in the crus on the same side as the ocular paralysis. Anesthesia of one side of the body with anesthesia of the opposite side of the face (crossed facial anesthesia) may be due to a lesion of the upper portion of the pons. Very rarely hemianesthesia is indicative of a lesion in the optic thalamus, or a large cortical or subcortical lesion of the parietal, temporal, or occipital lobes, or is associated with multiple sclerosis. An incomplete hemianesthesia of one side, with partial hemiplegia of the opposite side, may occur as a result of a unilateral lesion of the spinal cord. Spinal cord lesions cause irregularly distributed disturbances of light touch sensibility, especially important in the early diagnosis of spinal cord tumors

Bilateral anesthesia, sometimes amounting to a double hemianesthesia, but generally confined to the lower extremities and the lower part of the trunk, is rarely, if ever, due to a lesion of the brain It is an infrequent symptom in hysteria. Anesthesia of the lower extremities, if in conjunction with varying degrees of paralysis, is usually due to some lesion affecting the spinal cord such as an injury or compression of the cord by dislocation, fracture, or caries of the vertebrae; spinal menin-

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or may occur in multiple and scattered patches in any portion of the body Anesthesia of a single extremity rarely originates from a cerebral lesion, but when arising from this cause, the anesthesia is most marked at the terminal portion of the limb and gradually lessens as the trunk is approached; if caused by a spinal lesion, its proximal border will present a sharp line of demarcation In order to determine whether they are coterminous with the area of distribution of any of the peripheral nerves, the shape and location of isolated areas of anesthesia should be compared with a chart to find if they correspond to definite spinal segments. Single or multiple circumscribed patches of anesthesia are usually due to hysteria, neuritis or tabes dorsalis

An excessive sensibility to tactile and other impressions attends a considerable number of disease conditions and is termed *hyperesthesia*. Areas of hyperesthesia are of *frequent* occurrence in hysteria and constitute the so-called hysterogenic zones, for instance tender points on the thorax, the lower part of the abdomen and the back, pressure on which will excite and, if continued, may stop a hysterical parox-

ysm In neurasthenia there is a frequent hyperesthesia of localized points along the spinal column and on the scalp and thorax The scalp is often tender following headaches (especially of migrainous type) and facial or occipital neuralgias The area supplied by any neuralgic nerve may be temporarily hyperesthetic. The paralyzed side in a hemiplegia may be slightly oversensitive, and in some cases of brain tumor there is a marked and extensive hyperesthesia. In unilateral lesions of the spinal cord there is a narrow zone of hyperesthesia above the level of anesthesia on the side of the lesion

Disturbances of the temperature sense consist in a loss of the cold sense or the heat sense, or both, or a condition of reversal of sensation, cold being called hot and vice versa Such alterations from the normal are especially characteristic of syringomyelia and to a less extent of locomotor ataxia and lesions of the medulla.

Disturbances of the pain sense comprise *hyperalgesia,* an excessive sensibility to painful stimuli, and *analgesia,* a loss of sensibility to pain Analgesia is found particularly in syringomyelia and hysteria

Loss of the muscular, articular and tendinous senses constitutes ordinary, versus cerebellar, ataxia. It indicates an interruption of the sensory conduction tracts for such impressions It is seen especially in lesions involving the incoming sensory fibers, as in locomotor ataxia and Friedreich's disease. Disease in the ascending tracts, myelitic disease, compression, and occasionally lesions at the higher levels of the medulla and pons may cause it. Diffuse lesions, as in multiple sclerosis and paresis, may also be responsible for it.

Of these separate senses, loss of weight sense (muscular anesthesia) may be found alone in hysteria and cortical lesions, impairment of posture sense (articular and tendinous anesthesia) may be present in tabes and neuritis before ataxia is found; static ataxia involves muscular and articular sensation, and motor ataxia concerns articular and tendinous sensations

Astasia-abasia, inability to stand and to walk although the legs are otherwise under control, is generally a symptom of hysteria rather than a separate disease, and most commonly succeeds an emotional storm or an injury. It has been observed also in tabes, multiple sclerosis, spastic paraplegia, multiple neuritis and exophthalmic goiter It has been known to follow infectious diseases, carbon monoxide poisoning, overexertion in walking, and painful affections of the leg There is no paralysis, and while the patient is in bed the movements of the feet and legs show no in-co-ordination, but on attempting to stand or walk the legs give way. Women and young adults are commonly affected

Irregularities of sensation such as allochiria, which is a transference of sensation so that a touch on one side of the body is felt on the opposite side, may be present in hysteria, locomotor ataxia, disseminated sclerosis, and myelitis. Polyesthesia (a touch with one point felt as two) is of the same significance. Delayed conduction (tactile or pain), so that the response may require 10 seconds instead of one-tenth second, may be found, especially of pain, in locomotor ataxia and various peripheral paralyses Of similar moderate suggestiveness are after-sensation, an increasing pain lasting for some minutes after a pin prick, and double sensibility to touch and pain, in which the tactile impression is first perceived, the painful impression coming to consciousness after a varying time

Stereognosis is the power of recognizing the form or shape of objects when handled *Astereognosis* is the loss of this power, and is found in spinal or peripheral lesions attended by complete tactile anesthesia or loss of deep sensibility. In cerebral disease it is significant of a lesion (tumor, hemorrhage) in the parietal lobe, the center for deep sensibility and perception of form

In *paresthesia* the sensations of tingling and numbness may result from lesions of any part of the sensory pathway

In general, lesions of the peripheral nerves commonly affect all modes of sensi-

bility. Localized lesions of the spinal cord may impair some modes while leaving others intact. Thalamic lesions may involve all modes though not always equally. Cortical lesions tend to involve the spatial and discriminatory elements of sensibility.

Spontaneous pain as a result of central lesions characteristically occurs in connection with thalamic lesions. Severe and persisting pain may arise from relatively slight injuries when irritation is set up at the site of injury. Pain as the result of peripheral nerve injury may be of an intense burning quality and may be associated with dryness, redness and extreme hyperesthesia of the skin innervated by the affected nerve (causalgia).

The resulting disability from sensory loss varies and is difficult to evaluate The disability and disorder of movement ensuing on defects in postural sensibility are known as *sensory ataxia* There is an unawareness of the position of the lower limbs and of the range and direction of movements. The benefits of vision in control of these disorders are remarkable, for vision gives direction and, to some extent, control of movement. When the eyes are closed, or when the patient is in the dark, ataxia develops and the patient begins to sway and stagger, a phenomenon familiarly known as Romberg's sign. In the upper limbs, the subject has difficulty in distinguishing by manipulation the size and shape of objects held in the hand, and this is termed *astereognosis* The finger-nose test determines the presence or absence of postural sense in the upper limbs Have the patient endeavor, with eyes closed, to place the index fingertip on the nose. The arm deviates from its normal path, moves around in an uncertain way, and may fail to reach its objective.

In general, with cerebral disease, incontinence of either urine or feces is the result of disturbances of consciousness. The mental apathy associated with frontal lobe lesions often is accompanied by the passage of urine and feces These acts should be termed mental incontinence rather than sphincteral incontinence

In the semicomatose patient a distended bladder often leads to restlessness and indications of distress, and therefore the possibility of its presence is manifest. In acute transverse lesions causing total paraplegia there is retention of urine, followed by overflow, and finally by automatic micturition. The periodic sphincteral relaxation allows the escape of some of the vesical contents but not of all. There is always residual urine. In slowly progressive compression of the spinal cord the initial sphincteral disorder is followed by automatic micturition Acute retention of urine may suddenly develop in one of these bladders. The paralyzed bladder often becomes infected, and chronic infection leads to shrinkage of the organ and to almost continual dribbling of urine, and thus the condition grows worse In total paraplegia from transverse lesions of the cord periodic fecal incontinence occurs.

THE NONSENSORY SYSTEM AND LOCOMOTION

The pathways of the nonsensory stimuli seem to be the two spinocerebellar tracts of the cord These impulses arise in muscles, joints, bones and the labyrinths It is believed that these stimuli are integrated by the gray matter, which includes the red nucleus and [illegible] the cerebellum is the organ the functions [illegible] adjust movements and attitudes for har- [illegible] ut cortical directions.

DEEP SENSIBILITY

Mechanics of Visceral Pain. White states that observations on the pathways of visceral pain in man have revealed that there are sensory nerve endings in the viscera, particularly in the heart and intestine. The afferent axons, similar to those found in cutaneous sensory nerves, run in the autonomic nerves from the thoracic and abdominal organs to the posterior roots of the spinal cord These axons are anatomically and physiologically different from sympathetic and parasympathetic fibers which they accompany in the autonomic nerve trunks. These anatomic differences have

been correlated with knowledge gained from experimental stimulation of human viscera, the results of resection or chemical blocking of the various autonomic ganglia and trunks, and interruption of posterior spinal roots

There are pain-sensitive fibers in the vagus and pelvic parasympathetic nerves, and in the thoracolumbar sympathetic ganglia and splanchnic nerves

In malignant disease of the viscera intractable pain is often due to direct extension of the growth into the spinal nerves (see Autonomic Nervous System, Ch. 23).

Tenderness, which is a painful sensation produced by pressure, is slightly different from hyperalgesia. Hyperalgesia may be present without causing tenderness In some conditions of severe hyperalgesic pain, especially the colics, the patients find application of pressure, even a strong firm pressure, most gratifying. Sometimes there is dissociation between the tenderness of subjective pain and the pain itself, the tenderness being present over the site of the lesion, while the subjective pain may be limited to that region or may be referred to a distant region.

There are three painful reactions to pressure. (1) The pain is increased by pressure of any kind, and the lightest touch causes severe distress (2) The pain is increased by deep pressure only, this generally indicates some deep inflammatory lesion (3) The pain is increased by superficial pressure only. This is usually a manifestation of a psychoneurosis.

Rigidity of the underlying muscles is, as a rule, associated with tenderness and is the only good confirmative sign that pain is present Points which aid in differentiating the malingerer from the actual sufferer are the characteristic changes in respiration and pulse, both in rate and rhythm, that occur when pain is produced Often there are varying amounts of perspiration, especially of the palms of the hands

THE REFLEXES

The reflexes to be tested depend on the prevailing complaints and manifestations Generally and routinely some of the cutaneous or superficial reflexes, the tendinous or deep reflexes and, in certain instances, the organic or excitoreflex action are tested

All reflexes presuppose the traveling of a stimulus from the periphery along the afferent nerve to the motor cells in the cord or medulla The motor cells transform the received stimulus into an impulse which is reflected to the periphery along an efferent (motor) nerve to certain muscles, which in consequence contract involuntarily This reflex action ordinarily occupies from one twelfth to one tenth of a second The superficial or cutaneous reflexes are elicited by irritating the skin or mucous membrane, thus causing contraction of the muscles near the irritated part; the deep or tendon reflexes are produced usually by striking the tendon, but also by sharp percussion of the muscle or the periosteum near the tendon The organic or visceral reflexes involve a definite and co-ordinate response to special stimuli as, for instance, defecation

The Superficial (Cutaneous) Reflexes. The cutaneous reflexes are usually tested by sharply stroking the skin with a pointed object, or by scratching, tickling, pinching and pricking When accurately tested, the cutaneous reflexes are diagnostically important Table 6-1 gives a list of these superficial reflexes

The presence of a cutaneous reflex is of value because it demonstrates that the reflex arc (sensory nerve, spinal segment, motor nerve) on which it depends is normal

Of all the superficial reflexes the plantar reflex is of greatest diagnostic significance. In order to perform the test, the patient must be recumbent and the foot comfortably warm, while the limb should be partially flexed at hip and knee and at the same time rotated outward. The sole should then be gently stroked from the heel toward the toe (Fig 6-67).

In the normal person, in all periods of life after locomotion has been acquired,

bility. Localized lesions of the spinal cord may impair some modes while leaving others intact. Thalamic lesions may involve all modes though not always equally. Cortical lesions tend to involve the spatial and discriminatory elements of sensibility.

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The Deep or Tendon Reflexes. Tendon reflexes are the fundamental response of muscle tone. A tap on the tendon produces a momentary stretch, which in turn stimulates the sensory organs in the fleshy part of the muscle.

A tendon reflex is abolished by an interruption of its reflex arc, either on the afferent or on the efferent side and in total division of the spinal cord The reflex arc may also be interrupted where the afferent and efferent links of the arc meet at the synapse within the spinal cord, for example, as in an injury, a compressing tumor, or syringomyelia. The segmental localization of the reflex arc is made use of in determining the level of a lesion in the cord.

The tendon reflexes are obtained by delivering a quick blow to the tendon with the middle finger of the hand or preferably with a reflex hammer.

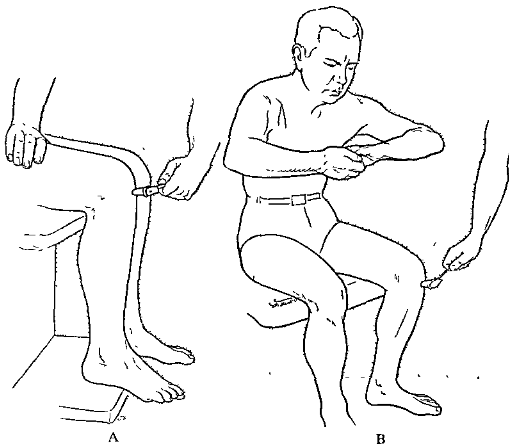


Fig 6 68 A, knee jerk Segmental level L_1, L_2, L_3, L_4 B, re-enforcement to enhance the reaction

In testing *knee jerk* the leg should be at right angles to the thigh (Fig 6-68A). The knees may be crossed, or the examiner may support the leg by placing his hand in the crook of the knee, or push his hand from the outside far enough under to rest it upon the opposite knee of the patient, thus letting the leg swing upon his forearm, or, if the patient cannot sit up, the legs should be slightly flexed and supported. The patient should be directed or diverted so that the leg is relaxed. A sharp blow (with edge of hand, finger, hammer) should be struck upon the tendon just below the patella. Under normal conditions there follows an abrupt jerk of the leg and

Table 6-1. The Superficial Reflexes

Reflex	Method of Eliciting	Response	Segmental Level
Conjunctival	Touch cornea (cotton)	Eyelid closes	Pons
Pharyngeal	Touch wall of pharynx	Pharynx constricts	Medulla
Palatal	Touch soft palate	Palate elevates	Medulla
Scapular	Stroke interscapular region	Scapular muscles contract	C_5 to T_1
Epigastric	Stroke downward from nipple	Epigastrium dimples	T_7 to T_9
Abdominal	Stroke down from costal margin	Abdominal muscles contract	T_{11} to L_2
Cremasteric	Stroke inner side of thigh	Testicle is pulled up	L_1 to L_2
Gluteal	Stroke skin over buttocks	Gluteal muscles contract	L_4 to L_5
Plantar	Stroke sole of foot	Great toe plantar-flexed	L_3 to S_2
Bulbocavernosus	Pinch dorsum of glans penis	Compressor urethrae contracts	S_3 to S_4
Superficial anal	Prick skin of perineum	External sphincter contracts	S_5 and conus

the great toe will be drawn into plantar flexion This reflex depends on continuity between the pyramidal tracts and the spinal reflex. Should the pyramidal tract be interrupted by any cause whatever, the reflex phenomenon is immediately changed, so that instead of plantar flexion there is plantar extension This plantar extension is known as Babinski's sign In infants, who have not yet acquired the skilled act of walking, Babinski's reflex is normally present. The reflexes of Oppenheim, Chaddock, and Gordon are but variations of, or bear the same significance as, the plantar response The segmental level of the plantar reflex is L_3 to S_2



Fig 6-67 Method of obtaining plantar response Segmental level L_3 to S_2

The palatal reflex may be lost in hysteria and bulbar paralysis The superficial reflexes in general may be absent on the affected side in the early stages of hemiplegia

The conjunctival reflex is elicited by touching the cornea with a soft material such as a wisp of cotton. The eyelid closes The reflex has its segmental level in the pons.

When the wall of the pharynx is touched, immediately the pharynx constricts. This reflex has its segmental level in the medulla The soft palate reflex is likewise in the medulla.

The scapular reflex is elicited by stroking the intrascapular region The muscles are seen to contract. The circuit is to C_5, C_6, C_7, C_8, T_1.

The epigastric reflex is obtained by stroking downward from the nipple. There is a quick visible response of the muscles The arc is T_7 to T_9

On stroking downward from the costal margin the abdominal muscles contract The abdominal reflex has its segmental level in T_{11} to L_2. [illegible] below

[illegible] L_2.

[illegible] its

The superficial anal reflex is obtained by pricking the skin of the [illegible] response is contracture of the anal sphincter. Its level is S_5 and below.

... of the calf muscles. Partly extend ... it in the hand seizes the front part of the foot (Fig. 6-70)' and abruptly pushes up or dorsiflexes it upon the leg. The calf muscles contract, forcing the foot downward against the examiner's hand, and if the latter continues to press steadily on the sole of the foot, a rhythmic, clonic movement of the foot will begin and continue. In some cases a very small amount of flexion and pressure will produce it True *ankle clonus must be distinguished* from the few clonic movements, rapidly ceasing, which may be observed as a result of similar manipulations in cases of neurasthenia and hysteria

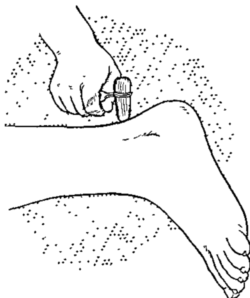


Fig 6-69 Ankle jerk Segmental level S_1, S_2

Paradoxical contraction is sometimes observed while testing for ankle clonus in a leg the muscles of which are extremely spastic It consists of a tonic contraction of the anterior tibial muscles produced by the abrupt dorsiflexion of the foot The segmental level of the ankle clonus is S_1 to S_2

Ankle clonus occurs in those conditions initiating hyperactive knee jerks and ankle jerks. *Often in a patient who has ankle clonus a similar clonus may be produced* by sharply pushing the patella toward the patellar clonus

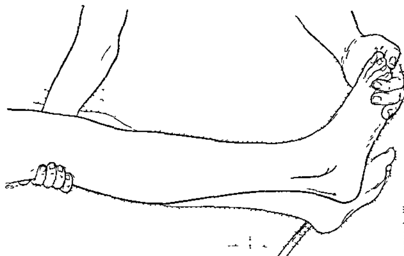


Fig 6-70 Ankle clonus The reflex is obtained while the patient is seated or lying with the knee slightly flexed

There are a few other tendon reflexes which may be used The *jaw reflex* is obtained by tapping the lower jaw directly with the hammer, or the blow may be cushioned as in Figure 6-71. The segmental level of the reflex is the pons. The jaw reflex is often absent in health It is not a significant reflex.

foot If it cannot be obtained, employ re-enforcement; for instance, request the patient to clench his fists strongly; or hooking his fingers together, to pull, one hand against the other, using all his strength (Fig. 6-68B). Either by lessening cerebral inhibition, or by causing an increase of the general muscular tension, re-enforcement may elicit an apparently absent reflex In some cases of exaggerated knee jerk it is possible to obtain a knee clonus equivalent to ankle clonus by fully extending the leg, seizing the patella, quickly pushing it downward and continuing the pressure. As a result the quadriceps may contract rhythmically for a considerable period.

The segmental level of this reflex is L_1 to L_4.

Absence of the knee jerk is caused by a lesion affecting any part of the reflex arc Like the other reflexes, presence of the knee jerk implies a healthy condition of the afferent (sensory) nerve, the posterior roots, the intraspinal paths, and anterior horn of the cord, the efferent (motor) nerve and the muscle itself. If the function of any portion or element of this circuit is in abeyance the reflex is modified Consequently, loss of the knee jerk is a symptom of disease affecting either the motor or sensory fibers or both. Knee jerks are usually absent in neuritis; disease of the posterior roots and columns—locomotor ataxia and Friedreich's disease; diseases of the anterior horns—anterior poliomyelitis (acute or chronic) and Landry's paralysis, and transverse myelitis, if affecting the second and third lumbar segments in which the reflex is localized Knee jerks are absent in apoplexy immediately after the shock, in epilepsy immediately after the convulsion, in injuries to the cord immediately after the accident, and in spinal meningitis. They are frequently lacking in the toxemias of diphtheria, diabetes mellitus (sometimes also insipidus) and chorea.

Exaggeration of the knee jerk shows that the reflex arc is intact, but that either the normal restraining influence of the upper (cerebral) motor neurons is destroyed by lesions affecting the cells, or their fibers which run down in the lateral pyramidal columns are destroyed; or that the irritability of the spinal cord as a reflex center has been increased. Consequently, taking the intracranial causes first, the patellar reflex is exaggerated in the hemiplegia of apoplexy on the affected side shortly, but not immediately, after the attack, in the cerebral paralysis of children, in hereditary cerebellar ataxia; and in general paralysis of the insane The lesions affecting the function of the pyramids are multiple, lateral and amyotrophic lateral scleroses Transverse myelitis, injuries to the spinal cord (after the immediate effects of the traumatism have passed), pressure on the spinal cord, and unilateral lesion of the spinal cord, if situated above the level of the second and third lumbar segments, will, by cutting off the inhibiting cerebral impulses, cause exaggeration of the knee and ankle jerks. If the lesion is unilateral, the exaggerated reflex will be on the same (paralyzed) side. The patellar reflex may also be exaggerated as a symptom of hysteria, neurasthenia, rheumatoid arthritis, tetanus, and strychnine poisoning.

The *ankle jerk* is usually present in health; ankle clonus is usually abnormal. Absence of the ankle jerk has the same, although less important, significance as absent knee jerk, exaggerated ankle jerk and the presence of the ankle clonus are of equivalent value to exaggerated knee jerk, the clonus being found especially in lateral amyotrophic and disseminated sclerosis A brief abortive or false clonus has been mentioned as occurring in neurasthenia and hysteria

In testing *ankle jerk*, extend the patient's leg and hold it up by grasping the foot, at the same time bending the foot upward so as to stretch the tendo achillis.

A better position is obtained by having the patient kneel on a pad or a pillow on a low stool or on the steps of the examining table. When in readiness, strike the tendon sharply and observe the resulting extension of the foot and the contraction of the muscles of the calf of the leg (Fig. 6-69) The segmental level of this reflex is S_1 to S_2.

response of the tendon reflexes in a limb, or between one side and the other, is often of diagnostic import when evaluated by an experienced examiner.

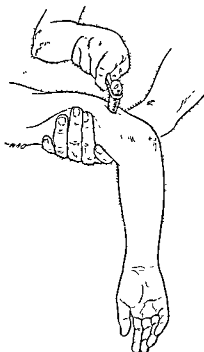


Fig 6-73 Triceps reflex Segmental level C_5, C_6, C_7

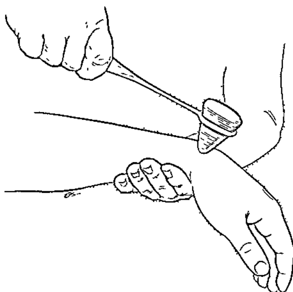


Fig 6-74 Supinator longus reflex Segmental level C_5, C_6

Muscle Tone and the Reflexes. Besides the many disturbances of the nervous system and in the muscles themselves, muscle tone may or may not be changed. If it is increased, it is termed hypertonus, and if it is decreased, there is a hypotonus or an atonia

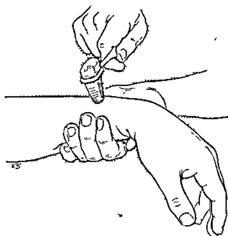


Fig 6-75 Carpometacarpal reflexes Segmental level C_6, C_7, T_1

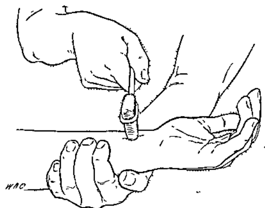


Fig 6-76 Flexor tendon reflex Segmental level C_6, C_7, C_8

A slight but general increase of muscle tone attends preoccupation or emotional states This fact is made use of in the procedure of re-enforcement when there is difficulty in eliciting the tendon jerks

The *scapulohumeral reflex* is obtained by tapping the inferior angle of the scapula. The reflex level is C_5 and C_6. The *supinator longus tendon at the wrist* when tapped by a reflex hammer causes a quick but perceptible contraction of the fingers. The segmental level is C_5 and C_6.



Fig 6-71 Jaw reflex Segmental level, the pons

The deep reflexes of the *upper extremities* are of much less diagnostic value than those of the lower extremities because they are frequently absent in health. The diagnostic significance of these jerks when present, allowing for the difference in localization, is the same as that of the knee jerk

The biceps reflex is obtained by tapping the biceps tendon as illustrated in *Figure 6-72. The reflex level* is C_5 and C_6 The triceps reflex is obtained by tapping the triceps tendon (Fig. 6-73). Its segmental level is C_5, C_6, C_7.

The supinator longus tendon reflex may be obtained by tapping the tendon at the wrist (Fig. 6-74) The segmental level of the reflex is C_5-C_6.

The carpometacarpal reflex is obtained by tapping the back of the wrist. The fingers are extended The segmental level of the reflex is C_6 to T_1 (Fig 6-75)

When the flexor tendons at the wrist are hit with a reflex hammer, the fingers are observed to be transiently flexed. The level of this reflex is C_6, C_7, C_8 (Fig 6-76).

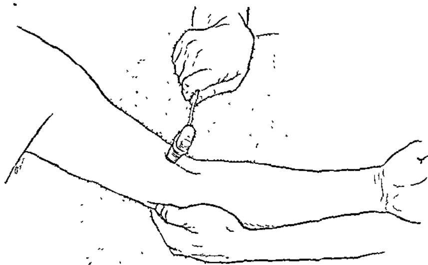


Fig 6-72. Biceps reflex Segmental level C_5, C_6.

The *abolition of a tendon jerk* may be associated with the appearance of an alternative response. This phenomenon is called inversion of the reflex. Inversion may be observed in injuries of the cervical portion of the spinal cord associated with damage to the fifth and sixth cervical vertebrae.

What constitutes a normal degree of briskness in a tendon jerk is judged by the experience of the examiner. The differences between the rapidity or sluggishness of

lesions commonly are found on the thorax, abdomen, neck, shoulders, thighs, buttocks and face. The lesions are unilateral and rarely involve more than three dermatomes. However, extensive eruptions do occur. Within 2 to 3 days after the zoster, a generalized cutaneous eruption resembling varicella may appear. Localized paralysis and atrophy in the muscles of the thorax or abdomen corresponding to the distribution of the eruption may develop These palsies are permanent in most instances. Symptoms of irritation of the parietal peritoneum or pleura or even of the urinary bladder may accompany zoster. Hiccough may occur in association with thoracic zoster.

Frequently some of the cranial nerves are involved by zoster. Affection and paralysis of the third, fourth and sixth nerves are rare. The gasserian ganglion and the first branch of the fifth nerve are frequently affected The eruption affects the upper eyelid, the conjunctiva and cornea and is accompanied by severe pain. The keratitis of zoster may leave permanent scarring of the cornea As the result of anesthesia a neuroparalytic keratitis may ensue. Optic neuritis and loss of vision have been recorded

A facial palsy and zoster of the external auditory canal and loss of taste may be associated The eruption of zoster may occur over the anterior two thirds of the tongue and the hard palate or the anterior pillars of the pharynx.

DIAGNOSIS The eruption of herpes zoster is characteristic The difficulty and the important diagnostic consideration are the differentiation of primary from secondary forms of the disease. The presence of any signs or symptoms which cannot be reconciled with the symptoms of the primary disease arouses a suspicion of some other nervous disease. A zoster may be the first intimation of metastatic malignant disease in or along the spinal column or the sequence of irradiation therapy.

The prognosis of primary zoster is good Herpes zoster of the gasserian ganglion may cause permanent damage to the cornea and in some cases the facial palsy associated with geniculate herpes may persist. The syndrome of crocodile tears may follow herpes of the ear As a sequela of facial nerve zoster there may be profuse lacrimation from the homolateral eye whenever food is taken

Tabes Dorsalis (Locomotor Ataxia) Tabes dorsalis, a manifestation of neurosyphilis, is commoner in men than in women. The disease is manifested from 5 to 20 years after the primary infection by *Treponema pallidum* (see Treponema in Chapter 17) Tabes dorsalis may result from congenital syphilis and may occur in childhood, adolescence or early adult life.

Regularly there is a low-grade inflammation of the posterior spinal ganglia, of the roots between the ganglia, the spinal cord and the meninges. A selective degeneration of the neurons of the posterior columns of the cord is characteristic There may be degeneration of the optic nerve and the nerves supplying the ocular muscles. The trigeminal and the vagus nerves occasionally are affected The nerve pathway which has to do with the pupillary reflex is almost always affected early, producing the Argyll Robertson pupil

SYMPTOMS As seen in the private practice of medicine, patients who have tabes dorsalis usually complain of symptoms which are often not referable to the syphilitic involvement of the spinal cord The disease is often diagnosed from the investigation which follows the discovery of an Argyll Robertson pupil and absence of knee or ankle tendon reflexes

If the patient seeks medical aid for tabes dorsalis, it is often because of disturbances of locomotion or for pain The locomotor disturbances are manifested by disturbances of the sense of position of the parts or losing balance on leaning forward The pain arises from injury by the syphilitic process to the posterior nerve roots and the spinal ganglia which are sensory in function The pain may be mild or severe. If mild, the pain is described in various ways; but generally, if severe, it is described as sharp, boring, shooting, lightning-like, lancinating, compressing

Muscle tone is increased in disease both of the pyramidal and of the extrapyramidal motor systems, but in each case the increase is qualitatively different The spasticity caused by an upper motor lesion is easily to be differentiated from the rigidity of extrapyramidal disease as, for instance, in Parkinson's disease. Both of these types of increased tone are reflex in origin and are abolished if the afferent nerve fiber from the muscle is severed and the reflex arc thus broken Muscle tone is estimated by the manipulation of the limbs to determine the sense of the degree of the active elastic tension in the muscle. The knowledge of the normal range of this tension can be gained only through experience

DISEASES MAINLY AFFECTING THE SENSORY NERVOUS SYSTEM

Herpes Zoster (Shingles, Zona). Herpes zoster is a specific infectious disease caused by the varicella-herpes zoster group of viruses. There are a selective inflammation of the posterior root ganglia and herpetic eruption within the corresponding dermatomes Trauma and diseases and irradiation which involve these ganglia may *cause eruptions of the same type and distribution. There are, therefore, a true* herpes zoster and a symptomatic type of zoster. The vesicles must be regarded as the result of disturbances of function of the ganglia and not as due to the localization of virus in the skin, for the disease cannot be transmitted to experimental animals by inoculation with the vesicular fluid It is thought that zoster is related to chickenpox, *since varicella sometimes develops in persons exposed to zoster and, conversely,* zoster may develop after exposure to varicella.

An attack of zoster confers a high grade of immunity. However, second attacks do occur.

Symptoms This disease occurs sporadically, and it is said to occur occasionally in epidemics in summer and autumn It is a weakly contagious disease It is sometimes possible to trace the infection to a contact.

The incubation period is between 1 and 3 weeks. The first symptom is pain accompanied with severe cutaneous hyperesthesia The pain corresponds *in its distribution* to one or more dermatomes and may be mild or intense There is often a low fever.

The herpes or shingles usually proceed halfway around the body or halfway across the forehead. The lesions are characterized by clusters of vesicles on an *erythematous base which appear in the region of the skin* disturbance of one or more of the posterior spinal nerves The onset of the disease is preceded by or accompanied with neuralgic pain, often very severe, and tenderness in the part. The erythematous patches, more or less oval with the long axis *parallel to the underlying* nerves, occur successively The number of lesions varies from two or three to several dozen Soon the surfaces of the patches are studded with papules which are quickly transformed into vesicles The important feature of the eruption is that it is unilateral. Herpes zoster frequently accompanies or is associated with varicella *However, an attack of varicella does not prevent the patient* from having herpes zoster. In herpes zoster of the forehead, the conjunctiva and the eyeball may be attacked and sometimes the mouth, the tongue or the palate may be affected

After 3 or 4 days erythematous patches appear within the area of *hyperesthesia* [illegible]
Then very [illegible]
spots. The [illegible]
disease is a [illegible]
spinal fluid often contains in excess of 100 lymphocytes per cubic millimeter.

The active phase *of the disease lasts only a short* time, usually a week or less As a rule, the pain persists in middle-aged and aged patients long after the eruption has healed. Hyperesthesia corresponding to the dermatomes involved may persist for years.

Shingles rarely appears on the extremities distal to the elbow or the knee The

any time during the course of the disease. Ocular palsies resulting in ptosis and strabismus and diplopia are common and are characteristically variable in their course However, they may be permanent. The other cranial nerves rarely give symptoms. Occasionally there is deafness. The vagus nerve may be involved, resulting in the so-called posticus paralysis, a bilateral paralysis of the abductors of the vocal cords.

Trophic ulcers, perforating ulcers, especially of the plantar surface of the toes and balls of the feet, are occasionally present. These ulcers are very deep and often penetrate to the bones. Syphilitic clubfeet as the result of involvement of bones and joints of the feet may be present.

Muscular atrophies are rarely encountered. Occasionally a foot drop, due to atrophy of the peroneal group of muscles, and, less frequently, atrophy of the tongue are present. Plantar extension indicates vascular neurosyphilis with involvement of the pyramidal tract, or a supervening general paresis, otherwise it is not present in tabes dorsalis

In the examination for tabes dorsalis, if the disease should be typically manifest, the columnae gracilis and cuneatus (Gall and Burdach) are affected These columns lie between the posterior horns of gray matter and the posterior septum They convey the senses of touch, position (proprioceptive sense) and vibration. However, some of the fibers for touch are in the anterior fasciculi If these posterior columns are affected, there is a flaccidity of the muscles and the joints and a positive *Romberg sign.*

In testing for the Romberg sign, request the patient to stand with the feet close together. If this is accomplished satisfactorily, the examiner stands behind the patient in a position of readiness to catch him if there should be evidence of loss of balance, and the patient is asked to close the eyes If there is more than normal swaying when the eyes are closed, the sign is positive and there is disease of the posterior columns Aside from the normal uncertainty in standing, in labyrinthine and cerebellar disease, the Romberg sign is negative in these disorders

Involvement of the sensory nerve roots by the syphilitic process produces objective and subjective sensory disturbances. The zones of hyperalgesia and hyperesthesia, of radicular distribution corresponding to the level of the nerves affected, are frequently situated in the midthoracic and the lower lumbar regions. There is absence of nerve trunk tenderness In rare instances the cutaneous distribution of the trigeminus nerve is affected, and thus paresthesias are present about the nose and cheeks

The deep sensibility is characteristically affected; the change is manifested by loss of sense of position of various members, for instance, of movements of the toes Early impairment of position and vibratory sensation is always found. This may be slight at first or may affect only the toes, or vibratory sensation may be lost only, over the sacrum In cervical tabes the process begins in the cervical segments so that the disturbance of position sensation and ataxia begin in the upper extremities

The serologic reactions of the blood are positive in from 60 to 75 per cent of those who have tabes The serologic reactions of the spinal fluid generally are positive As there is invariably some degree of meningeal inflammation, there usually is an increase of cells in the spinal fluid, anywhere from 10 to 100 per cubic millimeter This pleocytosis depends on the extent of the meningeal reaction, the acuteness of the process, the stage of the disease and the influence of treatment In quiescent forms of the disease there may be no cells in the spinal fluid, and serologic reactions may be completely negative The globulin content is usually increased The colloidal gold curve is tabetic

DIAGNOSIS An Argyll Robertson pupil is a sign of parenchymatous neurosyphilis, namely, tabes and paresis

In paresis an Argyll Robertson pupil is associated with prominent mental symp-

or squeezing. The attacks of pain are often paroxysmal, come on fairly suddenly, last a few hours, days or weeks, and cease abruptly, only to recur again and again Some patients are free from them, others are tormented by them throughout the course of the disease The distribution of the pain depends on the situation of the syphilitic process If the lumbosacral roots are affected, there are pains in the legs; if the lower cervical roots are involved, the pain is frequently along the ulnar side of the arm, if the lower thoracic roots are affected, the pains are in the abdomen The pain may be localized in the thorax or it may affect the trigeminal roots and simulate neuralgia

As the result of syphilitic injury to the sacral paths, there are complaints of disturbances in the genital, vesical and anal functions. Impotence and loss of libido in men and genital anesthesia in women may occur during the course of the disease. Paresis of the bladder (cord bladder), manifested by retention or incontinence of urine, may be complained of Relaxation of the anal sphincter, which may occur early in the disease, and anal incompetence with loss of feces are grave symptoms

Affections of the joints of trophic origin (Charcot joints) may occur in tabes These joint disturbances may appear after trauma, but because of the absence of pain, the patient is unaware of the seriousness of the injury. A trophic syphilitic joint never improves, the course is progressive. Charcot joints, as the result of destruction of the vertebrae, may permit of serious injury to the spinal cord The symptoms of cord injury are those of a transverse myelitis. Tabetic clubfoot may bring the patient to the physician. Spontaneous fractures of the bones resulting from the presence of gummas are rare.

The impairment of both superficial and deep sensibilities is characteristic of tabes dorsalis. Very early in the course of the disease there may be a feeling in the feet as if they were treading on a soft surface such as a carpet or velvet

During the course of tabes dorsalis there are often feelings of *euphoria*. The family may relate incidents and evidences indicating fallacies of the patient's judgment.

Examination. Ataxia is often present which depends on impairment or abolition of deep position sensation carried by the posterior columns. The ataxia is manifested by a sense of insecurity with uncertainty in walking This uncertainty causes steppage gait, in which each foot is raised higher than in normal gait and then is slapped flatly to the ground A tabetic patient would rather ascend a stairway then descend. There is great difficulty in walking in the dark. There may be bruises of the face or forehead On washing the face, if the patient closes the eyes, a fall forward and injury by striking the forehead against the wall may occur. As the ataxia increases, the tabetic patient walks with the feet farther apart in order to broaden the base of support The uncertainty of the gait is further manifested by the close watch the patient keeps on each step and the use of walking canes Muscular hypotonia is present. It may be so marked as to give hyperextension at the knees (*genu recurvatum*) and flat feet (*flaccid pes planus*).

Very early in tabes the deep reflexes are diminished, and then abolished Loss of knee jerks and ankle jerks is common to all tabetic patients and may even be the first sign and precede the other signs and symptoms by months or years The abdominal reflexes may be hyperactive

The pupillary reflexes are disturbed early. The disturbance may originate in the ciliary ganglion or the pathway between it and the primary visual center, in the centers themselves, in the nuclei of the third nerve or in the sympathetic pathways. The pupils may be miotic, irregular and unequal. They usually do not react to light, but do react during accommodation. This is the Argyll Robertson pupillary action. Once the Argyll Robertson pupil is present, it is permanent.

The ophthalmologist may be the first to announce the presence of tabes dorsalis. The optic nerve is commonly affected. Blindness from optic atrophy

Bilateral lesions produce bilateral anesthesia, and unilateral lesions cause the Brown-Séquard syndrome in which there are analgesia and thermanesthesia on the side opposite to the lesion and loss of proprioceptive sensibility on the side of the lesion If analgesia and thermanesthesia are found over an area corresponding to that of one or more dermatomes, with little or no loss of tactile sensibility, a lesion in the gray matter of the spinal cord is suspected.

Congenital Malformations Involving the Spinal Cord and Meninges. ***Diplomyelia.*** The term diplomyelia refers to doubling or duplication of the spinal cord. The duplication exists in the lower part of the cord and rarely if ever extends above the midthoracic region. There is no constant disturbance of function associated with diplomyelia In approximately half of all cases there is spina bifida of the occult variety. Other abnormalities are common and usually are grossly manifested.

Myelodysplasias. *Myelodysplasia with spina bifida* is a defective development of the spinal cord associated with defect in the overlying vertebral laminas.

In *complete rachischisis* the neural tube lies open and exposed for a number of segments. There is always paralysis.

Meningomyelocele is a rounded surface tumor containing the spinal cord which has retained its connection with the surface ectoderm and is attached firmly to the sac wall.

Meningocele is a bulging surface tumor covered with normal skin Within the skin is a sac composed of the meninges which may or may not be fused so that the sac has a single or a double wall

In *spina bifida occulta* the laminae of the vertebrae are defective. In rare instances the site of the lesion is marked by changes in the overlying skin, such as abnormal growth of hair, a dimple, a deposit of fat or telangiectases. In the majority of these persons there are no symptoms In an occasional individual, when the posterior surface of the spinal cord is attached to the meninges, paralysis is associated In other patients a progressive gliosis may develop and cavities appear in the gray matter, so that the symptoms are similar to those of syringomyelia

There is a malformation of the cervical spine in which the vertebrae are reduced in number and fused into one mass of bone. Spina bifida is usually present This condition is termed *myelodysplasia with Klippel-Feil syndrome*

Myelodysplasia may be associated with *absence of the sacrum and coccyx.* The normal prominences of the buttocks are lost and the intergluteal fold is also absent. Palpation reveals soft tissue where the sacrum should be Roentgenologic examination reveals the defect (Arey)

Myelitis and Abscess of the Spinal Cord. The staphylococci, and streptococci commonly, but occasionally other pyogenic organisms, may reach the spinal cord by way of the blood stream, by penetrating wounds or by direct extension from adjacent foci of infection, and thus originate a myelitis or an abscess.

The onset of the myelitis is often obscured by the presence of symptoms due to the primary infection It usually requires a severe pain in the back and the rapid development of a flaccid paralysis of the legs in order that the symptoms be noticeable or attributable to disease of the spinal cord In some patients the retention of urine is first observed On examination the tendon and the plantar responses are abolished. Sensibility is lost below the level of the lesion. In some instances there has been no serious illness The history reveals that there was a skin infection or trauma with infection which seemingly healed. After this the symptoms of a spinal cord tumor developed

The spinal fluid contains a variable number of leukocytes and lymphocytes depending on the degree of meningeal involvement Protein is almost always increased in the spinal fluid

The diagnosis is made by recognizing a transverse myelitis of rapid onset developing in association with septicemia or with a suppurative process.

toms. Other forms of neurosyphilis usually show a fixed pupil and *are characterized* by signs of disseminated lesions which come on much earlier in the course of syphilis, are much more acute in their onset, and also respond better *to treatment.* The Argyll Robertson pupil in a patient who has a history of primary or secondary syphilis, even in the presence of no other manifest symptoms, is almost diagnostic of tabes. The Argyll Robertson pupil in association with a history of pains in various radicular zones, or a diminished or absent knee jerk or ankle jerk or both, or a history of girdle sensation and vomiting, or the presence of ataxia, or a history of vesical disturbance with impotence, or disturbed position and vibratory sensation in the toes, and hyperesthesia over the nipples, buttocks and ankles, or loss of nerve tenderness, or early optic atrophy—any combination of these—is sufficient to establish a diagnosis of tabes dorsalis. Tabes dorsalis may be diagnosed in the absence of pupillary signs, provided there are signs and symptoms indicative of involvement of posterior roots and posterior columns accompanied with a positive serologic reaction for syphilis These symptoms and signs are pains, crises, loss of deep reflexes, and ataxia The presence of positive or of negative serologic reactions of the blood may influence an error in diagnosis A positive serologic reaction of the blood alone is not diagnostic A positive serologic reaction for syphilis in the spinal fluid is diagnostic if accompanied by appropriate signs and symptoms.

Differentiation of tabes dorsalis may be extensive because of the many possible manifestations of the disease. Some diseases to be differentiated are multiple neuritis (polyneuritis), combined sclerosis of the cord and Adie's syndrome

The etiology and pathogenesis of Adie's syndrome are unknown. The association of this syndrome with other disorders, such as influenza, polyneuritis, encephalitis, multiple sclerosis, orthostatic hypotension, vitamin deficiencies and endocrine disorders, particularly hypothyroidism, has been suggested However, the syndrome seems to be more frequently associated with nervous and emotional disorders. The syndrome is characterized by tonic pupils and sometimes absent tendon reflexes.

A tonic pupil is one having a delayed or slow response to accommodation and convergence. The pupil constricts more than the normal pupil under the same stimulus. It responds slowly to bright light and dilates in the same manner after the stimulus has been withdrawn The tonic pupil is usually unilateral, although it may be bilateral. The abnormal pupil is usually larger than the normal pupil The tonic pupil reacts normally to both atropine and physostigmine. The Argyll Robertson pupils, on the other hand, are usually miotic, bilateral and fixed to light stimulation but react promptly to convergence.

The tendon reflexes most frequently absent in Adie's syndrome are the Achilles and patellar reflexes, although all tendon reflexes may be absent In contrast to tabes dorsalis, the patient with Adie's syndrome has no loss or disturbance of vibratory or position sense, and none of the superficial sensory disturbances, lightning pains or gastric crises.

There are variations in the findings in Adie's syndrome Some patients have tonic pupils alone and others have absence of reflexes alone. In the intermediate positions are those having atypical pupils with absence of one or more tendon reflexes.

DISEASES OF THE SPINAL CORD

In association with the brain and its meninges the spinal cord and its meninges share in a number of infections due to bacteria, viruses, and higher plant and higher animal parasites. Here will be considered some of the diseases which often profoundly affect locomotion, namely, some of the more chronic infections, acute injuries, and metabolic, vascular, unknown and tumorous diseases of the cord and its covering.

Loss of sensibility on one or both sides of the body up to a level corresponding to the lower border of a dermatome indicates that a lesion is in the spinal cord

and impotence are frequent and persistent. There may be ataxia or chronic progressive spasticity.

There may be present pupillary signs, most often fixed both to light and on accommodation Ocular palsies are common If the process be limited to the region about the central canal, there may be a dissociation of pain and temperature sense as in syringomyelia

DIAGNOSIS A history of syphilis, positive serologic reactions in the presence of signs of meningeal reactions and cord changes, an increased number of cells in the spinal fluid, increased globulin and a positive colloidal gold curve are diagnostic of meningomyelitis. The serologic reaction of the spinal fluid may be negative.

The outlook in syphilitic meningomyelitis depends on the duration of the process, on the extent of involvement, and on the treatment. The disease is not cured, but symptomatically the patient may improve under proper treatment

Traumatic Lesions of the Spinal Cord. As the result of trauma the spinal cord may be injured without fracture or dislocation of the spinal column. The history of an injury to the vertebrae signifies the nature of the injury.

The roentgenologic examination will reveal fractured or dislocated vertebrae if they are present. In rare instances, however, no lesions of bone may be demonstrable roentgenologically. The anatomic character and severity of the lesion in the spinal cord frequently cannot be determined at once. If the paralysis is not complete at first, the injury is relatively mild, but if there is complete loss of conduction in the cord, it is impossible to say whether the cord is actually transected or whether there is a transient loss of function without complete anatomic dissolution

A sudden total transection of the spinal cord causes immediately total flaccid paralysis of the limbs, sensory loss, loss of tendon jerks, retention of urine, and sometimes transient absence of all plantar response There is spinal shock If the patient does not die from infected bedsores or cystitis, spinal shock passes off in a few weeks The knee and ankle jerks may return but the plantar response remains extensor. Stroking of the sole may produce involuntary passage of urine

When the lesion is incomplete, the reflexes return after a relatively short time and the muscle tone returns, chiefly in the extensor If signs of compression of the spinal cord develop weeks or months after an injury of the back, the following possibilities should be considered delayed traumatic spondylopathy associated with deformity of the spinal column due to collapse of a vertebra, osteomyelitis, tuberculous spondylitis, and, above all, the extrusion of an intervertebral disk.

Death in the first few hours may occur from paralysis of respiration, from shock or from associated injuries After the first few days the danger is chiefly from infected decubitus ulcers, infections of the urinary tract and pneumonia Lesions high enough to weaken the muscles of respiration cause a high mortality rate

The prognosis as regards recovery depends on the severity of the injury If the lesion is only partial, there is always much functional improvement

Kuhn and Macht have observed the involuntary activity patterns of skeletal muscles innervated below the level of severance in 27 instances of complete section of the spinal cord Some patients survived as long as 42 months The progression of reflex activity following spinal cord transection in this series of patients was. spinal shock, minimal reflex activity, flexor spasms, alternating flexor and extensor spasms and predominant extensor spasms The length of time that different subjects remain in a given stage varies considerably In general, stage 1 lasts for 1 to 6 weeks, stages 2 and 3, 6 weeks to 1 year, stage 4 rarely begins prior to 4 months after injury, and usually is terminated within 1 year, and stage 5 may appear as early as 6 months after the injury and may continue indefinitely Extensor thrust is not common, but can be elicited occasionally in spinal man Spinal standing, similar to that seen in animals with transected cords, can occur in spinal man Sustained patellar and ankle clonus frequently occurs in chronic spinal man Primary extensor

Pyogenic myelitis is almost invariably fatal. However, drainage of such an abscess, by Woltman and Adson, led to recovery.

Pyogenic Infections of the Spinal Epidural Space. Furunculosis caused by staphylococci is the commonest cause of infection of the epidural space. There is fever, as well as severe pain in the back which extends along the course of the spinal nerve roots. Flaccid paraplegia develops in about one week There are rigidity of the spinal column and local tenderness. The spinal fluid contains an excess of cells. Pus may be obtained from the epidural space when lumbar puncture is attempted.

The diagnosis of extradural abscess depends on the rapid development of paraplegia which usually ascends, on the rigidity of the spinal column, on the signs of an acute septic infection and, most important of all, on the discovery of pus in the epidural space.

The prognosis in cases of extradural abscess is very poor Antibiotic therapy is used.

Hemorrhagic Myelitis. Hemorrhagic myelitis is a secondary process due to various bacterial, viral and other poisons Any acute infectious disease may cause a hemorrhagic myelitis, for instance, scarlet fever, diphtheria, rickettsial disease, malaria, pneumonia and septicemia, to mention only a few

The symptoms are those of transverse myelitis, disseminated myelitis, or ascending myelitis with flaccid paralysis The tendon reflexes are lost, the plantar response is extensor, and there is retention of urine The paralysis of some of the muscles is permanent The disturbance of sensibility if present disappears within a short time

The mortality rate is high and averages between 30 and 50 per cent Death generally occurs between the fifteenth and eighteenth days and is associated with coma and bulbar palsy, bronchopneumonia and infection of the urinary tract Some of those who have the disease recover while others sustain a lasting disability

Syphilitic Meningomyelitis. Neurosyphilis produces syndromes which refer to the spinal cord, the brain or the meninges In each of these syndromes there are symptoms which indicate an obvious fact, that the entire nervous system is affected in neurosyphilis.

The changes caused by syphilis may be largely limited to the spinal cord alone or to the spinal meninges, generally it involves both. The infection very often begins in the meninges There are inflammation and fibrous thickening of the meninges and adhesions between the dura and piarachnoid which may contain granulations or gummatous tumors There are endarteritic changes, strangulated thrombosed vessels, and hemorrhage with secondary spinal softening and degeneration The inflammatory process may extend to the roots of the spinal nerves, causing atrophy of the nerve fibers When the syphilitic process affects mainly the spinal cord, there are softening and atrophy In the cord the process may be selective and remain largely restricted to the periphery, limited to certain columns and tracts, or it is partial, or complete at only one level of the cord. In other instances of cord involvement the process is diffuse and disseminated

SYMPTOMS. The meningovascular variety of neurosyphilis commences within the first 5 or 6 years of the infection There may be paraplegia, spinal hemiplegia, quadriplegia, or a Brown-Séquard syndrome. The paralysis is generally spastic but may be flaccid The syndrome may simulate that of subacute poliomyelitis with segmental atrophies and no sensory disturbances

There are often pains in the root zones. These pains are present in the neck, back or loins The pains are often girdle-like and follow definite paths along the arms or legs, and whether mild or severe they are worse at night than in the daytime. Spasms and atrophies of the muscles are present when the motor roots are affected *Meningomyelitis* occasionally is manifested by pains, ataxia and vesical disturbances, and severe headaches are common

EXAMINATION. There is a loss of tendon reflexes. Patchy sensory disturbances, a loss or diminution of sensation below the level of the lesion in the paraplegias, spinal hemiplegias, and quadriplegia are common. Vesical and rectal disturbances

the preservation of the axis cylinder accounts for the possibility of remissions. It is only when both the myelin sheath and the axis cylinder are destroyed that the signs and symptoms become permanent.

SYMPTOMS Multiple sclerosis may be manifested by disturbed functions in one or many different parts of the nervous system For instance, neurologists distinguish a *sacral* form of the disease characterized by sphincteric disturbances of the anus and bladder The *cervical* form of the disease is manifested by acute unilateral ataxia, astereognosis, slight spasticity, and sensory changes. In the *bulbar* form the process is characterized by disturbance in phonation, articulation and deglutition If there are disturbances of function of the facial and trigeminal nerves, the disease is designated as *pontine* multiple sclerosis. Asynergy characterizes a *cerebellar* form of multiple sclerosis. *Cortical* forms of the disease are rare, but when present the manifestations are acute hemiplegia and ophthalmoplegia There are, however, a number of signs and symptoms which occur with sufficient frequency and consistency to make multiple sclerosis a unified clinical disease.

A sufficient number of patients who have multiple sclerosis have scanning speech, tremor and nystagmus so that these constitute a triad of symptoms considered to be diagnostic of the disease. However, these are but a few of the symptoms usually present in the disease

The first symptoms, such as a fleeting ocular palsy manifested by temporary strabismus or a slight visual disturbance, or a mild leakage of urine or a transient weakness of a limb, often signify the onset of multiple sclerosis months or years before the patient is aware that a serious disease is developing

A disturbance of locomotion, manifested by difficulty in walking, often is the first definite symptom. The gait becomes spastic or ataxic and there is increasing hypertonicity of the lower limbs. Often the patient stumbles or falls in walking. The greatest in-co-ordination is often in the upper extremities. Acute ataxia of an arm alone may occur.

In rare instances the onset is acute and is manifested by apoplexy The syndrome is ushered in by hemiplegia, at times accompanied by unconsciousness and, rarely, even by a convulsion In rare instances, too, the illness is that of a transverse myelitis, in these, however, the acute symptoms usually recede.

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There may be difficult micturition or slight transitory incontinence Vesical incontinence occurs when there is severe involvement of the sacral segment of the spinal cord Anal incontinence is rarely present

Emotional disturbances such as an impulsive laughter, more rarely crying, often occur early.

EXAMINATION In the early stages of the disease, in the interim between attacks, results of examination may be negative

Coincident with or preceding the development of spasticity, the knee jerks and ankle jerks become hyperactive Plantar extension and clonus are present (Babinski sign). There are early impairment and loss of the abdominal reflexes. Loss of abdominal reflexes accompanied with an ataxic tremor with an intention element are pathognomonic signs of the disease. The tremor comes on gradually, usually in the upper extremities, and frequently becomes extreme. It may become so disturbing as to interfere with dressing and eating. The tremor usually disappears at rest and is absent during sleep

Lateral nystagmus is an early and common sign of multiple sclerosis. It indicates a focus in the medulla or pons

There may be areas of hypalgesia and hypesthesia, or even complete loss of

manifestations in chronic spinal man probably represent the reappearance of primitive and poorly integrated postural activity mediated by the isolated cord, the functional capacity of which seems greater than has been assumed Although spinal man passes through a period in which flexion reflexes alone are active, he may frequently progress to a stage of activity characterized by predominantly extensor reflexes, amounting in many cases to extensor spasm. It is probable that many of the discrepancies between these observations and those of earlier investigators can be explained by the better physical conditions of present-day spinal men.

Circulatory Diseases of the Spinal Cord. The intraspinal blood supply is derived from the central or anterior sulcal branch of the anterior arterial trunk and the peripheral arteries arising from the pial plexuses These two systems, although possessing anastomosis of capillaries, function as end-arteries The arterial distribution is not according to anatomic or physiologic relations The larger vessels pass into the cord and supply the ganglion cells

The veins emerging from the interior of the spinal cord are united into extensive venous plexuses on the surface upon which are situated the main longitudinal channels

Occlusion of the Anterior Spinal Artery. When the anterior spinal artery is occluded, there are sudden paraplegia, absence of defense reactions, dissociated pain and temperature sensory disturbances accompanying disturbances of vesical and intestinal functions. These symptoms vary according to the level involved Flaccid muscle paralysis and segmental atrophy ensue.

Atherosclerosis. Atherosclerotic changes in the blood vessels may be present in the spinal cord, and are most intense in the thoracic part of the cord. Likewise in syphilis the upper thoracic part of the cord will be most affected by syphilitic arteritis

Mild but distinct evidences of degeneration of the posterior column and horn appear in vascular disorders of old age.

In generalized atherosclerosis, signs of defective nutrition of the cord appear under stress or exertion similar to what occurs in the brain Like that of the brain, the anemia of the cord is intermittent in character.

The most frequent symptom is numbness and a feeling of coldness in the lower extremities There is a diminution or loss of vibratory and joint sensibility, and sometimes the sense of touch is impaired There may be local muscular atrophies and spasticity

The effect of atherosclerotic changes in the vessels supplying the peripheral nerves is to decrease the blood supply to the peripheral nerves as well as to the other tissues There results the so-called arteriosclerotic neuritis. The symptoms consist of marked pain, hyperesthesia of the skin, atrophy and glossiness of the skin and occasionally some objective sensory changes and muscular atrophy.

Disseminated (Multiple) Sclerosis. Multiple sclerosis is a chronic intermittent disease of the central nervous system. Remission of a part or all of the symptoms may be short or may last over a period of years. Usually, however, there are repeated relapses with steady aggravation and progression of all signs and symptoms until invalidism and death result.

Multiple sclerosis is essentially a disease of early adult life, in most cases occurring between the ages of 20 and 40 years. The disease is commoner in men than in women

The constant pathologic features of multiple sclerosis consist mainly of numerous and widespread foci of sclerosis of varying ages of duration throughout the central nervous system, degeneration of the myelin sheath and preservation of the axis cylinder in the midst of the foci of sclerosis (periaxial neuritis).

The sclerotic process is situated more in the white matter of the spinal cord, especially the pyramidal tracts, and in the structures of the medulla, pons, midbrain, and the optic chiasm and tract. Owing to the varying ages of the patches of the sclerosis the patient may be observed to have some signs and symptoms which remain permanent and others which are capable of remission

Degeneration of the axis cylinder proceeds until it is finally destroyed The destruction of the myelin sheath alone permits of only a partial impairment of function, while

the preservation of the axis cylinder accounts for the possibility of remissions. It is only when both the myelin sheath and the axis cylinder are destroyed that the signs and symptoms become permanent.

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sensation. Disturbance of deep sensation, such as position and vibration, are found if the disease affects the posterior columns. Astereognosis may be profound

Ophthalmologic examination often reveals a bitemporal pallor of the optic disks and central scotomas Optic atrophy may produce blindness. However, all of these visual disturbances of the eyes, including total blindness, may show remissions

Ocular palsies with strabismus and double vision occur early or at any time during the course of the disease. Any disturbance of pupillary reactions, however, is not due to multiple sclerosis. Internal ophthalmoplegias are rare in multiple sclerosis

Bulbar and cranial nerve manifestations are rarely present. Occasionally paralysis of the vocal cords, disturbances of phonation, chewing and swallowing, and facial paralysis and deafness may occur

The spinal fluid in multiple sclerosis may show a slight lymphocytosis and a paretic gold curve. The spinal fluid pressure and globulin concentration are within normal limits The serologic reactions are negative

Diagnosis Increased tendon reflexes, spasticity of the lower extremities, plantar extension (Babinski sign), tremor, nystagmus, speech disturbance, ataxia, impulsive laughter, central scotomas, bitemporal pallor and negative serologic reactions in a patient who has had these symptoms remittently for a long time are diagnostic of multiple sclerosis

Combined Sclerosis (Ataxic Paraplegia) Combined sclerosis is a progressive disease of the spinal cord which most frequently results from pernicious anemia The disease may appear in the course of pernicious anemia in the absence of severe anemia It may advance to a paraplegic state

There is degeneration of the posterior and lateral columns of the spinal cord

The disease often commences with paresthesias, which are prominent throughout its course Involvement of the posterior columns gives varying degrees of ataxia of the lower extremities and occasionally of the arms The legs are almost always involved first There is frequently pseudoathetosis of the fingers

The tendon reflexes are often absent and vibration and position sensation are impaired or lost In instances of degeneration of the pyramidal tract there may be hypertonia with increased reflexes and finally a spastic-ataxic paraplegia The sensory disturbances may affect all forms of sensation Incontinence of urine and bedsores attest the severity of the cord involvement late in the course of the disease.

The onset of paresthesias, ataxia, disturbed vibratory and position sensation, diminished deep reflexes, and the presence of plantar extension and paraplegia, accompanied with pernicious anemia are diagnostic Pellagra may give an ataxic paraplegia, but this is a true myelitis

Syringomyelia (Spinal Gliosis). Syringomyelia is thought to be the result of an embryonic defect of development Under normal conditions the primitive glial cells migrate peripherally from the vicinity of the central canal of the spinal cord and differentiate into adult glial cells Probably in syringomyelia spongioblasts fail to migrate and eventually proliferate and thus form dense regions of gliosis in the central portions of the cord which later turn into cavities One or more cavities are present in the region of the cervical enlargement but may be present or extend to any segment of the spinal cord Occasionally the process begins in the lumbosacral enlargement rather than in the cervical region. The cavities from their points of origin in regions of gliosis in the gray matter near the central canal invade the anterior gray matter and the lateral columns or compress these structures

[illegible] the medulla oblongata (syringobulbia) there is a narrow slit-like [illegible] om the fourth ventricle and involving the [illegible] the descending root of the fifth nerve and perhaps the tractus solitarius Median slits are rare.

Men and women past the age of 20 years are affected with equal frequency. It is very rare for more than one instance of the disease to appear in a family.

SYMPTOMS The patient may complain of having burnt a foot or a hand in water too hot for bathing without knowing it until after the burn was sustained. Some muscles or groups of muscles may twitch and may have become weak, shrunken, or perhaps paralyzed The fascicular twitchings of the muscles progress up the arm as the muscles become weak and shrink. If the symptoms of weakness and shrinkage of the arms have been present for some time, paraplegia may have occurred, and the patient is confined to the bed and to the wheel chair.

Pain is not a common symptom in syringomyelia. Occasionally, however, there may be severe localized pains which involve one or both lower extremities. In some the pain is due to the scoliosis and is relieved by supporting the spinal column

EXAMINATION. On examination many and diverse findings are likely to be present which are widely scattered and which may be difficult to classify. The immediately noticeable abnormalities are atrophy and fibrillary twitchings of the affected muscles, deformities of the fingers and hands, and perhaps scoliosis in the thoracic region of the spinal column. The gait is unsteady and station is uncertain. There is paralysis in association with atrophy of the muscles, with loss of reflexes and flaccidity which usually occur first in the hands or arms. Involvement of the intrinsic muscles of the hands causes various deformities of the fingers After the fingers are involved, atrophy affects successively the muscles of the forearm, arm and the shoulder girdle The muscles of the neck, spinal column and thorax become atrophic toward the end of life. Fascicular twitchings in the affected muscles may be present. The muscular atrophy is not symmetric. In advanced instances of the disease there are paraplegia and spasticity of the legs There is a loss of sphincteral control

In some instances changes will be present in the joints of the upper extremities which are identical with the Charcot joints of tabes dorsalis. There are destruction of the cartilage and articular surfaces and relaxation of the capsule and ligaments, so that an abnormal range of movement is possible The bones may also become decalcified, causing spontaneous fractures. Local overgrowth of bones may occur, and the hand may resemble that of acromegaly.

When the lumbosacral part of the spinal cord is the situation of the syrinx, the atrophy and weakness begin in the feet, calves, thighs or hips Irregularities of sphincteral control in these patients are an early symptom

There are changes in the skin and soft tissues. The skin may be dry and thick, or thin and glossy. The thick nails may become opaque and shed Cyanosis, edema and ulcerations may occur on the fingers, causing extensive loss of tissue.

There is a loss of pain sense; tactile sense is not seriously disturbed In some instances all modalities of cutaneous sensibility may be lost in certain regions. The distribution of the anesthesia is variable. It may be bilateral as the result of interruption of the dorsal commissure It may be unilateral as the result of interruption of the posterior horn of gray matter. Sometimes the anesthesia involves the hand or the hand and forearm, presenting the so-called glove or sleeve anesthesia. In most instances the anesthesia is confined to the arms, shoulders, neck and thorax As the process in the cord advances and the posterior columns of the cord are affected, ataxia, loss of proprioceptive sensibility, unsteadiness of station and gait and finally complete anesthesia may develop over the lower half of the body

When the disease involves the cervical enlargements from extension from either side, there are often signs of involvement of the cervical sympathetic nerve, such as Horner's syndrome or unilateral sweating of the face. The descending root of the fifth nerve may be affected, causing analgesia and thermanesthesia of the face

Nystagmus is an indication of invasion of the medulla The tongue becomes atrophied and paralyzed on one or both sides The soft palate and pharynx and the vocal cords are often paralyzed The sixth nerve may be involved When a syrinx from the medulla reaches the cervical segments, there is paralysis of the sterno-

cleidomastoid and trapezii muscles, owing to invasion of the spinal nucleus of the eleventh nerve.

DIAGNOSIS. The diagnosis depends on the presence of a thermo-analgesia, a slowly progressive atrophy of the muscles supplied by the cervical enlargement, accompanied with dissociated anesthesia in the cervical dermatomes, the scoliosis and the trophic changes The presence of a syrinx in the lumbosacral enlargement causes identical signs in the corresponding segments

The differential diagnosis consists of the exclusion of progressive spinal muscular atrophy, leprosy, Raynaud's disease, cervical ribs with compression of the cervical nerve roots, and neurosyphilis.

Syringomyelia is sometimes accompanied by cervical ribs, and if the symptoms happen to be confined to the hand, the diagnosis may be in doubt until the extension of the symptoms is sufficient to make the nature of the process obvious

The disease may progress so slowly that the patient may be active for many years. As a rule, however, syringobulbia pursues a relatively short course. In all instances the prognosis is ultimately grave.

Tumors of the Spinal Cord. Tumors of the spinal cord cause locomotor difficulties by compression of the cord Compression of the cord, aside from that due to trauma, may arise from a decrease in the size of the bony conduit through which the cord passes; for instance, (1) from lesions of the vertebrae, (2) from space-occupying lesions of the meninges or nerve roots and (3) from tumors arising within the substance of the cord itself

In lesions of the spinal cord the attention is directed to the symptoms and the findings which help to determine the segmental level of the lesion and the structures involved in the transverse direction at the level affected When a disease is due to involvement of a neuron system it is designated as a simple systemic disease. When a disease affects more than one neuron system, as in amyotrophic lateral sclerosis, it is designated a combined neuron disease

In degeneration of the intramedullary continuation of the posterior roots of the spinal nerves, as occurs in tabes dorsalis, the cutaneous sensibility and the sensibility of the bones, joints, fascia and muscles are disturbed. Anesthesia for all qualities of sensation or elective losses of one or more sensations may be present The reflexes are lost There is in-co-ordination of movement of the muscles but muscle power is not diminished. The function of the bladder may be impaired or lost

Diseases of the sensory neurons of the cord are distinguished from lesions arising in the peripheral nerves by topography of the sensory disturbance in the peripheral nerve lesions which corresponds to the domain supplied by the peripheral nerve rather than to a distribution corresponding to the domain supplied by a posterior nerve root in a cord lesion

It must be recognized that knowledge alone of the motor, sensory, reflex and visceral representation in the segments of the cord does not permit diagnosis of focal localization or situation of a gross level lesion in the spinal cord Experience is required in order to evaluate and correlate findings with such facts as, for example, that a peripheral motor nerve innervating a given muscle rarely, if ever, arises from a single segment but, through the mediation of plexuses, has its origin in a combination of fibers from the anterior roots of spinal nerves. That is, each muscle has a plurisegmental innervation, and the innervation of muscles of the extremities is by nerve segments at a higher level

Generally extradural sarcomas are most frequent in childhood Intradural meningiomas are commonest among adults. Gliomas of the cord are relatively common Kernohan considers that gliomas of the spinal cord are the same as the cerebral gliomas He describes ependymomas, spongioblastomas, astroblastomas, medulloblastomas and ganglioneuromas. They usually arise in the central gray matter and extend over a number of segments of the cord.

SYMPTOMS. Tumor of the spinal cord commences *with pain, localized and persistent*, associated with cutaneous hyperesthesia at the level of the tumor. The pain is unilateral at first but may become bilateral or girdle in distribution. It is precipitated by coughing, sneezing and lifting If the cauda equina is involved, pain and muscle spasm on flexing the back are severe Often the pain becomes much worse shortly after the patient falls asleep in the reclining position. In children night crying after going to sleep is frequent. In adults pain disturbs or prevents sleep

EXAMINATION The findings on physical examination depend on the stage of development and the situation of the tumor. There may be either spasticity or flaccidity. Flaccid paralysis develops when the anterior surface of the cord is compressed In these lesions an ataxic gait and a positive Romberg sign soon follow. Cutaneous anesthesia below the level of the lesion is not long delayed after loss of proprioceptive sensibility. The anesthesia may begin in the dermatomes just below the level of the lesion and spread down, but more commonly it begins in the lower part of the body and extends slowly upward until it reaches the level of the pain. All modalities of sensibility are affected, but unequally on the two sides of the body. A more severe anesthesia is likely to be on the side opposite the weaker leg.

A lesion situated cephalad to the cervical enlargement of the spinal cord is manifested by muscular hypertonus including the diaphragm and the intercostal muscles Paralysis of respiration may occur. Lesions situated in the cervical enlargement cause paralysis of the arms, thoracic muscles and legs, but not the diaphragm. Lesions situated cephalad to the first thoracic segment may cause Horner's syndrome. The arms and the legs are paralyzed. Tumors of the thoracic segments of the cord cause spasticity and paralysis of the legs Tumors between the thoracic segments of the cord and the lumbosacral enlargement cause spasticity and weakness of the legs. One leg is affected more than the other Only the legs and the sphincters are affected when the lesion is situated in the lumbosacral enlargement.

A tumor of the cauda equina in some patients causes severe pain which extends along the course of the sciatic nerves The pain is increased by flexion or extension of the spinal column, coughing, sneezing, straining and by certain postures The patient may be comfortable when standing but may have intense pain when lying or sitting Loss of control of the bladder develops early The paralysis is flaccid

There are other patients who have a tumor of the cauda who only have pain and spasm of the flexor muscles of the knee, hip and lumbar portion of the spinal column The lumbar lordosis is reduced and the patient walks with the knees semiflexed Anesthesia is present over the buttocks and the posterior surface of the thighs and legs

In all spinal cord tumors pains in the body below the level of the lesion are usually absent Burning, tingling or hot and cold sensations are common. By the time definite anesthesia is present, there is likely to be difficulty in passing urine A loss of sphincteral control is a late symptom of compression of the spinal cord *Loss of control of the bladder occurs before rectal incontinence Toward the end the legs* become spastic and are strongly extended, a state which terminates in paraplegia-in-extension, followed by paraplegia-in-flexion Trophic changes in the skin and decubitus ulcerations may be present

Before any fluid is removed the *intraspinal pressure* is estimated, it normally registers between 12 and 15 cm. of water As soon as the pressure has been estimated, jugular pressure is applied. Sudden rise and rapid fall of the fluid on compression of both internal jugular veins indicate free flow of cerebrospinal fluid within the subarachnoid space Slow rise and fall of fluid or its failure to rise on compression of the jugular veins suggests partial or complete intraspinal block.

Inability to obtain fluid at the fourth lumbar interspace usually signifies that the tip of the needle has failed to enter the subarachnoid space, that fluid is absent or that there is a tumor at this level

cleidomastoid and trapezii muscles, owing to invasion of the spinal nucleus of the eleventh nerve.

DIAGNOSIS. The diagnosis depends on the presence of a thermo-analgesia, a slowly progressive atrophy of the muscles supplied by the cervical enlargement, accompanied with dissociated anesthesia in the cervical dermatomes, the scoliosis and the trophic changes. The presence of a syrinx in the lumbosacral enlargement causes identical signs in the corresponding segments.

The differential diagnosis consists of the exclusion of progressive spinal muscular atrophy, leprosy, Raynaud's disease, cervical ribs with compression of the cervical nerve roots, and neurosyphilis.

Syringomyelia is sometimes accompanied by cervical ribs, and if the symptoms happen to be confined to the hand, the diagnosis may be in doubt until the extension of the symptoms is sufficient to make the nature of the process obvious

The disease may progress so slowly that the patient may be active for many years. As a rule, however, syringobulbia pursues a relatively short course In all instances the prognosis is ultimately grave.

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plurisegmental innervation, and the innervation of muscles of the extremities is by nerve segments at a higher level.

Generally extradural sarcomas are most frequent in childhood Intradural menin-[illegible] are commonest among adults Gliomas of the cord are relatively common [illegible] mas
[illegible] nd
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In consideration of the symptoms of mononeuritis, it is realized that most peripheral nerves are mixed nerves; that is, they contain both sensory and motor fibers. The interruption by disease or section by trauma of a peripheral nerve causes paralysis of the muscles innervated and also sensory loss or changes in the skin innervated by the same nerve. In disease rarely is all of the nerve destroyed; when some parts of the nerve are still intact, there are manifestations of irritative phenomena in addition to aberrations of sensory function Motor irritative phenomena are spasms of the muscle. first small areas of the muscle which are termed fascicular or fibrillar twitchings and later contractures of the paralyzed muscle. In about three weeks atrophy of the flaccidly paralyzed muscle ensues

The sensory irritative phenomena are mainly pain, limited to the distribution of the affected nerve and described as hot, burning, scalding, throbbing or shooting in character. Paresthesia, dysesthesia, causalgia and tenderness along the nerve are common.

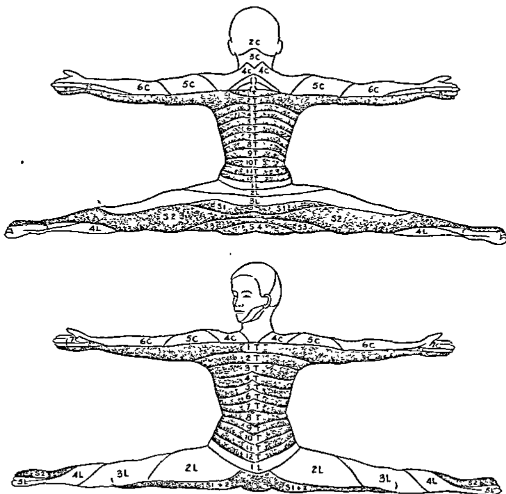


Fig 6-77 Cutaneous distribution of the spinal sensory nerves After Pottenger, F M, Clinical aspects of abdominal pain, J A M A, 102 341 (Feb 3, 1934). Redrawn with permission of the author, who credited Luciani's sketch from Bolk's data, and the publisher.

Neuritis may occur in any one of the spinal nerves. The cutaneous distribution of the spinal nerves is shown in Figure 6-77 Muscular atrophies following injuries of the spinal nerves may be present.

Spinal block, if it results from tumor, frequently causes an increase in the concentration of globulin in the cerebrospinal fluid below the tumor. The fluid may also be xanthochromic. The shade of yellow may vary, and occasionally the fluid above a block is decidedly yellow. The cell count is usually normal, but pleocytosis may occur if the tumor is situated in the spinal canal below the conus medullaris This may help in distinguishing neoplasms from inflammatory lesions

The presence of partial or total subarachnoid block is not pathognomonic of intraspinal tumor, since previous attacks of meningitis, acute myelitis, injuries to the vertebrae or spinal deformities are all capable of interfering with the free flow of cerebrospinal fluid.

Roentgenograms are made of anteroposterior and lateral aspects of the vertebral column, supplemented by stereoscopic and oblique views, localized at the level where a tumor has been suspected In general, roentgenologic evidence of changes resulting from tumors of the spinal cord consists in shadows indicative of erosion of the vertebrae secondary to direct pressure, invasion by the tumor, destruction caused by benign or malignant tumor of the bone, metastatic diseases or hyperostosis.

In addition to the roentgenologic evidence of tumors which is apparent in routine examination of the spinal column, roentgenoscopic and roentgenographic study by the use of radiopaque oil has furnished much additional information in diagnosis and localization of intraspinal tumors. However, radiopaque oil should be used only when tumors are suspected, and the oil should be removed whenever possible.

The manifestations of metastatic lesions may be the same as those of any benign tumor of the spinal cord, except that the progress of a malignant growth is more rapid than that of a benign tumor Metastatic growths from carcinomas of the breast or the prostate gland are most frequent. It must not be forgotten that a primary carcinoma of the breast may have been removed many years before metastasis gives evidence of its presence

Diagnosis If there is demonstrated a level which limits distally the occurrence of both sensory and motor disturbances, a single tumor of the spinal cord is probably present. This lesion may be primary in the cord or secondary to a malignant lesion elsewhere in the body In the presence of such findings there is a history compatible with that of tumor of the spinal cord Special roentgenologic studies should be made by those who are skilled in such procedures, and the roentgenograms should be interpreted by one skilled in such interpretations

When benign or malignant tumors can be removed completely, the outlook is *good, provided the operation is performed early and the cord is not traumatized.* Generally, however, the outlook is unfavorable despite the treatment

DISEASES OF THE PERIPHERAL NERVES

Lesions of the peripheral nerve trunks are common causes of locomotor disability. Each peripheral nerve trunk has motor and sensory components. When the nerve is sectioned, there is a complete loss of both of these functions Partial or progressive lesions which involve these component functions will vary.

There are distinctions to be made in the diseases of the peripheral nerves, the plexuses of nerves, and the nerve roots When disease affects the nerve or the nerve trunk, it is designated as neuritis, the plexus, as plexitis; and the nerve roots, as radiculitis.

Disease of the nerve trunks of the spinal nerves occurs as mononeuritis and polyneuritis The mononeuritis is said to be an interstitial neuritis, whereas the polyneuritis is caused by parenchymatous changes However, several nerves may be affected by mononeuritis The causes for mononeuritis and plexitis occurring in one or several nerves are infections such as leprosy, syphilis, trauma, serum sickness, ... (Reck-

Injury of the Brachial Plexus. The common type of brachial plexus injury is Erb's palsy, which results from strong traction on the shoulder in the delivery of the head in breech delivery, or from drawing of the head and neck away from the shoulders in the effort to deliver the shoulders in cephalic presentations. The paralysis is present immediately after birth

There are adduction and internal rotation at the shoulder, extension at the elbow and often pronation of the forearm and some degree of flexion of the wrist. When the arm is passively abducted, it falls limply. The flexors of the elbow and external rotators of the shoulder are inactive. The grasping reflex is intact In mild injury there is no weakness at the wrist. The biceps and radial reflexes are abolished As a rule it is impossible to demonstrate any loss of sensibility If recovery is delayed, contractures soon develop in the antagonists of the paralytic muscles unless prevented The head of the humerus becomes flattened and the margin of the acromion process becomes depressed in such a way as to prevent complete abduction.

The *distal type* of brachial plexus palsy is less common It involves the intrinsic muscles of the hand with weakness of the long flexors of the wrist and fingers. The grasp reflex is absent There is edema of the hand and there are trophic changes in the nails Loss of sensibility may be demonstrated in the hand. The pupil is smaller than the opposite one and the homolateral eyelid droops, although it can be opened. The iris may remain unpigmented (Fig 6-79).

Complete paralysis of the entire arm and complete loss of sensibility almost up to the shoulder may be present. There is partial arrest of development of the affected arm which is most evident in the hand (Fig 6-78).

Various bone injuries may be associated with brachial plexus palsies such as a fracture of the neck of the scapula, fracture of the clavicle, of the shaft of the humerus or separation of the epiphysis when they are due to postnatal trauma.

Supernumerary cervical ribs may cause abnormal relationships in the neck and lower roots of the brachial plexus. However, supernumerary cervical ribs usually do not give rise to symptoms. The symptoms of root compression may be due to pressure by a first rib when no supernumerary ribs are present. Cervical ribs may be found in several members of a family and have, indeed, been traced through a number of generations (Macklin)

The *symptoms* of root compression rarely arise before the age of 20 years Despite the fact that the ribs are almost always bilateral, the symptoms are almost invariably unilateral Drooping of the shoulders from poor muscular tone, paralysis of the trapezius, or wasting illness may precipitate the symptoms Women are affected three times as often as men. The right arm is more likely to be involved than the left

On *examination*, there is weakness of the hand and forearm with atrophy of the intrinsic muscles of the hand and of the superficial flexors of the wrist and fingers. Paresthesias, numbness and loss of cutaneous sensibility are found over the ulnar half of the hand and inner margin of the forearm The pain and thermal sensibility are reduced without demonstrable loss of tactile sensibility

The radial pulse may be small or absent. In order to test for the presence of circulatory disturbances in a patient who has a cervical rib or ribs, Allen, Barker and Hines recommend that the patient be seated with the arms extended horizontally with the elbows flexed until the forearms are perpendicular to the arms. The head is turned as far as possible away from the side being examined. A positive result of the test is indicated by diminution or disappearance of the radial pulse.

Occasionally the subclavian artery may be spontaneously occluded, resulting in gangrene of the fingers Manifestations resembling those present in syringomyelia or in Raynaud's disease are not uncommonly present in the scalenus anticus syndrome associated with cervical ribs.

Lesions of Peripheral Nerves. Small areas of analgesia surrounded by a larger area of tactile anesthesia suggest lesions of the peripheral nerves. The size and location of the area indicate the nerve or nerves affected. *Traumatic injuries*, either laceration or pressure palsy, are painless. Interstitial neuritis is accompanied by severe pain and by tenderness of the nerve trunks. Incomplete lesions of the peripheral nerves cause such syndromes as *causalgia*. Symmetrically distributed tenderness of the calf muscles and nerve trunks and cutaneous anesthesia or hyperesthesia over the distal parts, which fade out gradually over the more proximal parts, are significant of polyneuritis.

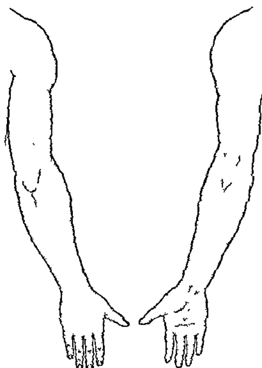


Fig. 6-78. Area of sensory changes in lesions of the brachial plexus (C_5, C_6, C_7, C_8, T_1)

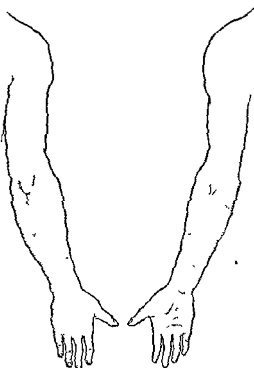


Fig 6-79 Area of sensory changes when the lower part of the brachial plexus is affected (C_8, T_1)

Sensory changes in an area of the skin known to receive its nerve supply from a given nerve corroborate the finding of a weakened or paralyzed muscle, or muscles, innervated by this same nerve. In the diagrams the bordering areas are not depicted. The limits of disturbances of light touch are included in the shaded areas, which merge into the areas where sharp or dull cannot be differentiated

The Brachial Plexus. The brachial plexus, a great nerve plexus of the neck and axilla, is formed by the union of the anterior branches of the lower four cervical nerves and the first thoracic nerve. It supplies the whole upper extremity, and its chief branches are the posterior thoracic, suprascapular, subscapular, internal cutaneous, musculocutaneous, musculospiral, circumflex, median, and ulnar nerves

The muscles supplied by branches of the brachial plexus and methods of testing have been given (pp. 201 and 202). (Nerve supply, C_5, C_6, C_7, C_8 and T_1.)

Sensory Changes in the Skin in Lesions of the Brachial Plexus and Peripheral Nerves of the Arm. In Figure 6-78 are depicted the areas of sensory [illegible] The level of segmental [illegible] ver roots, C_8-T_1, of the brachial plexus are affected, is shown in [illegible]

Fig 6-83 Area of sensory changes of the hand Ulnar nerve distal to origin of its dorsal branch

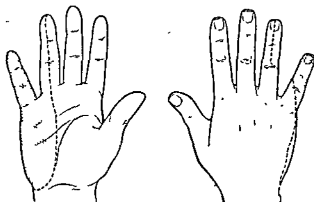


Fig 6-84. Maximal area of sensory changes in skin of the hand *observed in lesions proximal to the origin of the dorsal branch of the* ulnar nerve

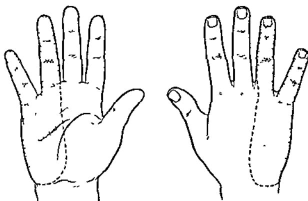


Fig 6-85 Maximal area of sensory changes of hand observed in lesions of the median nerve

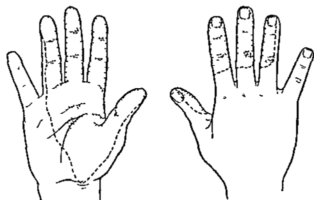
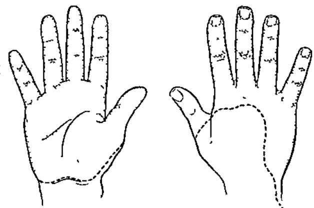


Fig 6-86 Sensory changes in hand when both median and ulnar nerves are affected



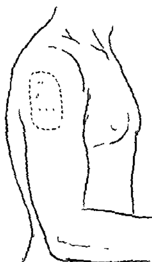


Fig 6-80. Area of sensory changes which attend injuries of the axillary nerve (C_5, C_6)

In *diagnosis* the roentgenographic demonstration cervical ribs in association with slowly developing atro of the muscles of the hand, pain and other disturban of sensation and pulse volume are confirmative.

Sensory Changes in the Skin Resulting From sions of the Peripheral Nerves of the Arm and Ha The area of distribution of sensory change, when *circumflex (axillary) nerve* is injured, is revealed in Fig 6-80. If the lesion involves the axillary nerve too, th will be paralysis of the deltoid muscle.

The *radial nerve* may be injured proximal to its bran the dorsal antibrachial cutaneous nerve. When the ne

brachial cutaneous branch and the musculocutane nerve is injured too, a combined lesion exists. The sens changes in the skin are diagrammed in *Figure 6-82*. T radial nerve also is the *motor nerve* to the brachioradi (C_5 and C_6); extensor carpi radialis supinator (C_5, and C_7); triceps (C_6, C_7); extensor digiti communis; extensor digiti V propri extensor carpi ulnaris; abductor pollicis longus; extensor longus, and exten proprius and extensor pollicis *brevis muscles* (see *Muscle Testing* of the Arm a Hand, pp 213 to 220).

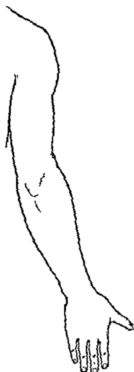


Fig. 6-81 Area of sensory change in injury of the radial nerve proximal to the dorsal antibrachial cutane-

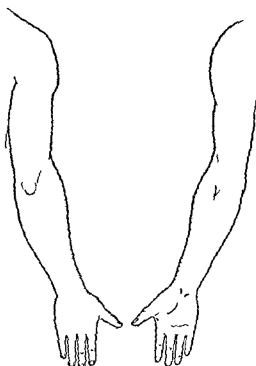


Fig. 6-82. Area of sensory change in injury of the radial nerve distal to the dorsal antibrachial cutaneous nerve

The approximate area within which sensory changes may be present in disturbances of the *posterior cutaneous nerve of the thigh* is revealed in Figure 6-90.

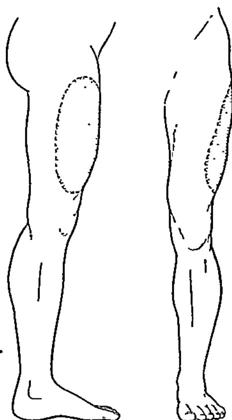


Fig 6-89. Areas of sensory changes in lesions of the lateral femoral cutaneous nerve (L_2, L_3).

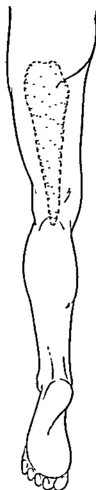


Fig. 6-90. Area of sensory changes in injuries of the posterior cutaneous nerve of the thigh (S_1, S_2, S_3)

The approximate area within which sensory changes may be detected in lesions of the trunk of the *sciatic nerve* is revealed in Figure 6-91.

The area within which sensory changes occur in lesions of both the *sciatic* and the *posterior femoral cutaneous nerve* is revealed in Figure 6-92.

An area within which sensory changes may be revealed in lesions of the *lateral popliteal (peroneal) nerve* above the origin of its musculocutaneous branch is shown in Figure 6-93.

An area within which sensory changes are present in lesions of the *deep peroneal nerve* is shown in Figure 6-94.

Sensory changes in lesions of the *sural nerve* are within the area revealed in Figure 6-95.

The area of sensory changes in lesions of the *medial popliteal or tibial nerves* is revealed in Figure 6-96

The cutaneous changes observed in the skin of the hand or injuries of the ulnar nerve depend on whether the injury is situated distal or proximal to the dorsal branch of the ulnar nerve. When the lesion is situated distal to its dorsal branch, the skin changes are shown in Figure 6-83. When the lesion is situated proximal to its *dorsal* branch, the maximal area of cutaneous changes over the hand ensues (Fig. 6-84).

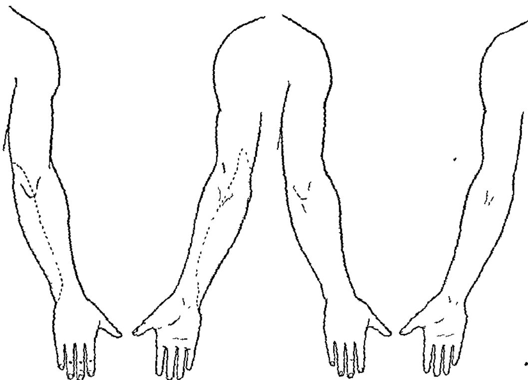


Fig 6-87 Area of sensory changes resulting from injuries of the medial antibrachial cutaneous nerve. Origin, brachial plexus

Fig 6-88 Area of sensory changes resulting from injuries of the lateral antibrachial cutaneous nerve

The ulnar nerve is the motor nerve to the flexor carpi ulnaris, lumbricales III and IV, flexor digitorum profundus, adductor pollicis, flexor digiti brevis V, opponens digiti V, abductor digiti V and interossei muscles of the hand (see Muscle Testing of the Arm and Hand, pp. 213 to 220)

The *median nerve* supplies sensory fibers to the skin of the hand; when maximal injury has been sustained by this nerve, the areas of sensory changes are revealed in Figure 6-85

When both the median and the ulnar nerves are injured, the area of sensory changes over the hand is revealed in Figure 6-86.

The median nerve is the motor nerve to flexor carpi radialis, pronator *teres*, [illegible] s, *flexor* [illegible] *pollicis* [illegible] *d Hand*, pp. 213 to 220).

Injuries of the median cutaneous nerve of the forearm cause sensory changes in [illegible] 6-87 [illegible] earm (a *branch* of [illegible] 6-88.

[illegible] of the Peripheral [illegible] Foot. The area within which sensory changes may *be found*

Allergy. Occasionally polyneuritis develops in association with serum sickness. The muscles supplied by the fifth and sixth cervical roots are usually most severely affected.

Physical Agents. A large variety of poisons may cause polyneuritis Lead neuritis is perhaps the commonest form. Arsenical neuritis was formerly common but has been rare since the medicinal use of arsenic has been discontinued Some of the sulfonamide derivatives may cause severe polyneuritis.

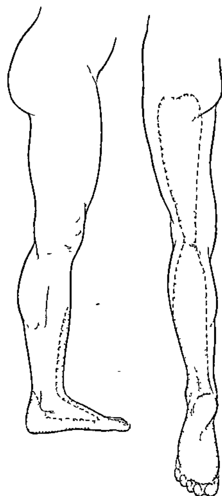


Fig 6-92 Area of sensory changes when the posterior femoral cutaneous nerve and the sciatic nerve are both affected

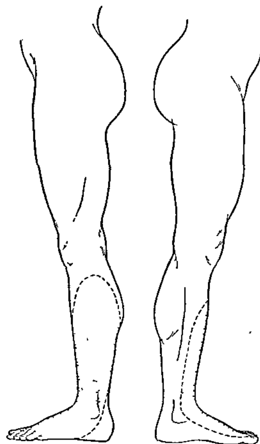


Fig 6-93 Areas of sensory changes in lesions of the common peroneal nerve.

Diabetic neuritis is often clinically latent—that is to say, the patient may not make any complaints, but examination reveals tenderness of calf and plantar muscles and absence of the ankle jerks In more severe diabetic neuritis, pains in the legs reminiscent of the lightning pains of tabes may be complained of, the knee jerks may be lost, and the degree of postural sensory loss may produce an ataxic gait and lead to an erroneous diagnosis of tabes dorsalis

Polyneuritis may be associated with acute *porphyrinuria,* hemochromatosis and amyloidosis

It is thought possible that chronic alcoholism and the cachexia of malignant disease and of chronic tuberculosis may lead to defective absorption of the relevant vitamins This is not substantially proved

Lesions of Spinal Roots. If the spinal roots are injured, the sensory loss corresponds to the distribution of the posterior roots and a radicular anesthesia The area of tactile anesthesia is smaller than that of relative analgesia and there is often so much overlap of the tactile fibers that even in extensive root lesions anesthesia cannot be demonstrated. For instance, in neuritis of the brachial plexus there is usually no anesthesia, but there are usually much pain and tenderness and cutaneous

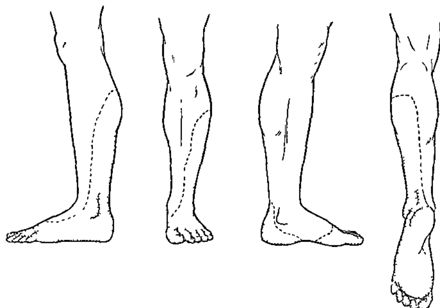


Fig 6-91 Area of sensory changes in lesions of the sciatic nerve (trunk) Origin L_4, L_5, S_1, S_2, S_3

hyperesthesia. Herpes zoster causes relative anesthesia over one or more dermatomes The pain may be relatively widespread, but the anesthesia, if present, is confined to the general region of the cutaneous lesions. The postherpetic neuralgia often causes much suffering in elderly persons See Figure 6-77, page 373

Radiculitis. Radiculitis is defined as an inflammation of the root of a spinal nerve. Usually the greatest part of the inflammation is situated between the spinal cord and the intervertebral canal The spinal cord is somewhat movable in the spinal canal so that when the spinal column is flexed, the cord rises slightly and when it is extended, the cord sinks backward When there is meningitis or radiculitis, flexion of the neck or elevation of a forcefully extended leg causes pain. The Lasègue, Kernig and Brudzinski signs are based on the presence of radiculitis

In radiculitis, as in neuritis, irritative phenomena of the motor nerves occur There are fascicular twitchings which may end in atrophy of the muscles involved if the irritation is progressive or is long-continued

Irritative phenomena of the sensory root are manifested by pain.

Polyneuritis (Multiple Peripheral Neuritis) Multiple peripheral neuritis or polyneuritis is a bilaterally symmetric affection of the peripheral nerve trunks to the limbs which involves both motor and sensory fibers. In some instances cranial nerves may be affected.

Infections. Infections are the commonest cause of polyneuritis In childhood, diphtheria is responsible for a large percentage of all cases It is usually recognized by the [illegible] In the [illegible] ia [illegible]

may also be associated with polyneuritis.

SYMPTOMS. The various etiologic forms of polyneuritis do not differ essentially in their symptomatology. The variation comes in the rapidity of development of the original disease and of recovery from it. Special symptoms which have been described as being peculiar to an etiologic variety of polyneuritis are symptoms of the original disease

The symptoms common to all forms of polyneuritis are the manifestations of a paralysis of lower motor neuron type. The legs are affected earlier and more severely than the arms The muscles below the knee and distal to the elbow are more severely affected than the proximal muscles There is drop foot and in severe instances wristdrop The muscles are tender to pressure In long-standing polyneuritis wasting and contractures and deformities ensue.

EXAMINATION. There are diminution and, later, loss of tendon reflexes All forms of sensibility are impaired, varying in degree and, like the paralysis, maximal over the distal extremities The trunk is rarely involved Early in the severely acute polyneuritis there is tachycardia. In some instances there is cardiac dilatation, and even fatal syncope.

DIAGNOSIS. The diagnosis is made from the findings on examination. If possible, the diagnosis should indicate the etiologic agent.

Acute Febrile Polyneuritis (Landry's Paralysis) Acute febrile polyneuritis differs in no essential from what is described as Landry's paralysis The term Landry's paralysis indicates an acute spreading and often fatal paralysis characterized by the absence of severe or constant changes in the nervous system.

Landry's paralysis and acute febrile polyneuritis commences by a brief period of febrile disturbance with headache, malaise and sleeplessness Often gastrointestinal disorders may precede the appearance of the paralysis The paralysis, which develops rapidly, is of a lower motor neuron type, flaccid, with loss of tendon jerks. Commonly there is paresthesia in toes and feet accompanying the development of paralysis, which spreads up the legs and often involves the arms. The abdominal and back muscles and the facial muscles may be affected The muscles of respiration are less severely weakened than the limb and facial muscles, except in fatal illness.

A pulse rate increase above 110 to 120 is a serious prognostic omen

If the patient does not die, the paralysis begins to diminish, clearing first in the muscles least severely weakened A general debility and exhaustion ensue The tendon reflexes slowly reappear

Interstitial Neuritis or Perineuritis. Interstitial neuritis is a local inflammatory reaction involving chiefly the interstitial connective tissue of the nerve trunk which is distinguishable from the generalized degenerative process of polyneuritis.

There are interstitial neuritides which are associated directly with active foci of infection and others which are not so associated An interstitial neuritis may be directly associated with arthritis, abscesses, lymphadenitis, nasal sinusitis, otitis, cellulitis, erysipelas, tonsillitis, infected teeth and septic ulcers In many instances, when the nerve lies in proximity to the site of infection, the inflammation reaches it by direct lymphatic extension

Debilitating infections such as pneumonia, typhoid fever or influenza may be followed by interstitial neuritis

The mechanism of production of an interstitial neuritis without direct association with foci of infection is not clear

The process commences by inflammation and swelling of the nerve which then becomes dense as the result of proliferation of connective tissue. The axis cylinders are not severely affected

The symptoms begin with deep and superficial pain which follows the course of the nerve trunk and is projected into the region of cutaneous distribution. The pain is sometimes constant but more often intermittent and paroxysmal The disease is extremely chronic

On examination it is observed that movements and postures which serve to place

Nutritional Disorders. It is well known that vitamin deficiency, more especially deficiency of vitamin B, will cause polyneuritis Walshe believes that "Beriberi is probably induced by a toxic product formed in the course of the disordered carbohydrate metabolism that ensues when carbohydrates are consumed in large quantities without the

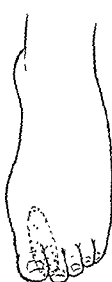


Fig 6-94

Fig 6-94 Area of sensory changes in lesions of the deep peroneal nerve



Fig 6-95

Fig 6-95 Area of sensory change in lesions of the sural nerve

normally occurring natural vitamins with them. Some as yet unknown component of the vitamin B complex is essential to the carbohydrate metabolism of the nerve cell. Despite the clinical evidence at hand, there are yet important gaps in the chain of evidence linking B avitaminosis with the development of polyneuritis"

The role of ethyl alcohol in the etiology of polyneuritis may be associated with lack of vitamin B.

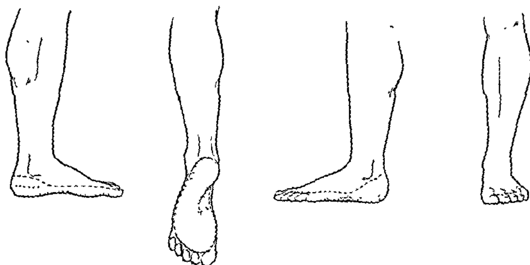


Fig 6-96 Area of sensory changes in lesions of the tibial nerve

Constantly disorders of function in instances of acute polyneuritis precede structural changes since there may be complete or relative absence of visible changes in the nervous system in certain rapidly fatal instances of multiple neuritis such as beriberi and Landry's paralysis. In long-standing, fatal multiple neuritis degenerative changes of wallerian type are found in the axis cylinders of the affected nerves The nerve cells and fibers of the cerebral cortex may also show a degree of degenerative change. The heart shows infiltration with fat and myocardial degeneration.

and is partially anesthetic. The nerve trunk which supplies the region of the lesion begins to become enlarged and palpable Various signs of neuritis slowly develop.

EXAMINATION. On examination the usual findings in leprosy comprise some one or many of the following: The fifth nerve frequently is affected. There may be patches of anesthesia over the forehead, the bridge of the nose and the cheeks which are associated with regions of depigmented skin, and macular, nodular (tuberculoid), or ulcerating nodular cutaneous lesions.

The *maculae* of leprosy involve the corium of the skin, particularly the hair follicles and the sweat glands. The bacillus of leprosy is difficult to demonstrate in these lesions. The *tuberculoid lesions* of leprosy occur as discrete ulcers separated by normal tissue. As the disease advances, these nodules may become continuous masses, pushing other structures aside as they expand With the expansion of the lesions the skin is thinned, and hyperkeratinization with scaling and hypopigmentation, or white spots in the skin, develops

At this stage of the disease the patient loses first the ability to discriminate between heat and cold, next sensibility to pain, and finally, tactile sense.

Frequently the anesthesia is bilateral and sometimes it is symmetric. Neuroparalytic keratitis may ensue All modalities of sensation may be affected but with a certain amount of dissociation. The degree of dissociation of cutaneous sensation, observed in syringomyelia, is not present There is usually palpable thickening of the superficial nerve trunks, especially of the supra-orbital nerve Localized palsies of the facial muscles are common and characteristic The ulnar nerve and the common peroneal nerve are affected early in the course of the disease. Atrophy and weakness appear in the intrinsic muscles of the hands and feet and slowly give rise to various types of flexion deformity including the so-called Simian hand. The ankle jerk and finger reflexes are lost and the knee and biceps reflexes are preserved. The plantar response is abolished and the abdominal reflexes are preserved

Disorders of vasomotor and secretory function and trophic disturbances are constant The hands and feet are cold and blue Sweat secretion is lost and the hair often falls out Dry necrosis of the fingers may be present, but it is commoner to find concentric atrophy of the small bones of the fingers and toes, so that the digit grows smaller and shorter Neuropathic joints are sometimes present The ends of the digits may slough away and leave only stumps of the fingers

The nasal mucous membranes are frequently affected, often with early perforation of the nasal septum. The mucous membranes of the tongue, pharynx and larynx may be involved Involvement of the conjunctiva, cornea and iris which leads to blindness is frequent The liver and spleen frequently are enlarged, and the secondary deposit of amyloid or amyloidosis is exceedingly common in the late stages of this disease Amyloid involving the kidneys gives the symptoms of nephritis

DIAGNOSIS. A definite diagnosis of leprosy must be based on finding of the bacilli in the nasal secretions or in the skin lesions Material aspirated from affected lymph nodes will often reveal the bacilli. For diagnostic purposes, a person who has thickening of the skin around the forehead, eyes, nose and lips, accompanied by other cutaneous lesions, enlargement of lymph nodes in the inguinal and axillary regions, and regions of anesthesia over the extremities or regions of anesthesia with rather severe pain in the arms or legs, has leprosy

The differential diagnosis of leprosy involves the following conditions: cutaneous syphilis, nasal or oral leishmaniasis, yaws and Boeck's sarcoid, Recklinghausen's disease (the form described as forme fruste) and syringomyelia

Nodular leprosy is likely to run a more rapid course than neuritic leprosy and to lead to death within 10 years Neuritic leprosy usually lasts longer Spontaneous remissions are described.

Alcoholic Neuritis. The first symptoms of alcoholic neuritis are cramps and pains in the calf and plantar muscles at night. There may be aching and fatigue in

the affected nerve under tension increase the pain. The nerve trunk is tender, and the tenderness is most severe over the inflamed segments. Sometimes the nerve trunk is palpable. In severe and prolonged instances of the disease there are paralysis and atrophy of the muscles, loss of reflexes and anesthesia

A diagnosis of interstitial neuritis or perineuritis requires history and evidence of a severe or debilitating infection or of neuritis if the tenderness is confined to the nerve trunk and if stretching the nerve causes pain Roentgenographic examinations are of value in excluding diseases of the bones and joints. A conservative prognosis is always given.

Leprosy. Leprosy is due to infection by an acid-fast bacillus, *Bacillus leprae* (*Mycobacterium leprae*), which morphologically resembles the tubercle bacillus.

Regularly in the neural or anesthetic type of leprosy the peripheral nerve trunks have nodular thickenings as a result of proliferation of connective tissue and cellular infiltration. The bacilli are sometimes present in large numbers in the innermost lamellae of the perineurium and in the endoneural septa. The number of bacilli is independent of the degree of tissue reaction In some cases the reaction is relatively acute with active inflammatory reaction and edema, but as a rule the process is chronic and the thickening of the nerve is due chiefly to fibrosis

Degeneration within the posterior roots and of the exogenous fibers of the posterior columns occurs relatively often The posterior root ganglia may be the seat of degeneration and of fibrosis Nonspecific degenerative changes in the brain have been described

In the cutaneous form of leprosy there are firm intradermal and subcutaneous nodules over the face and other exposed surfaces Ulceration and secondary infections are common Mutilation of the parts is due mainly to trauma from lack of sensation and to ulceration secondarily infected In all forms of leprosy lesions usually develop in all organs except the voluntary muscles The cartilage of the nose may be destroyed. The mucous membranes of the mouth, nose and eyes are badly injured. The lymph nodes may enlarge and become granulomatous The testes are often destroyed. Nephritis is common

Distribution Leprosy probably arose in Central Africa It is common in the Balkans, Asia, Asia Minor, India, China, Siberia, Africa, Iceland, Japan, Australia and the Philippines In the United States small numbers of cases are found in the Gulf region, along the Pacific coast and in the Great Lakes region.

Leprosy is common among children whose parents have the disease. If the children are removed from their parents immediately after birth, the incidence of the disease is low Congenital leprosy is rare. Infection is thought to be acquired through the skin or through the nasal mucosa, and to reach the skin by way of the blood stream The incubation period of leprosy is unknown

Two varieties of leprosy, the nodular form and the maculo-anesthetic or neuritic form, are described However, mixed types are common

Symptoms The early symptoms of leprosy may be the same, irrespective of the form of the disease which is about to develop. Irregular fever, sweating, weakness and epistaxis may be present, or a local cutaneous lesion may appear without other symptoms

In the nodular form erythematous lesions develop on the face, forearms, thighs and buttocks which become indurated nodules and eventually ulcerate However, there appear on the skin some spots which are often hyperesthetic at the onset but eventually become anesthetic Nodules appear on the mucosa of the upper part of the respiratory tract, and in the conjunctiva and cornea The ulcerations progress and great mutilations appear, as the result of trauma and secondary infection, and extend These mutilations are the basis for the classic descriptions of the disease.

In the maculo-anesthetic form the cutaneous lesions develop singly rather than in successive outbreaks. In these the macular lesions are white or yellowish and attain 1 to 3 inches (about 2.5 to 8 cm.) in diameter. These depigmented spots appear on the limbs, trunk or face They often have an erythematous border. Often there is neuritic pain at the onset. The skin affected by the macules does not sweat

voluntary control after complete palsy is accompanied by an increased muscle tone After the nerve has regenerated, an asymmetry of the face may remain. This asymmetry is not evidence of incomplete regeneration but evidence that nerve fibers have been misdirected and there thus remains a disturbance of function.

The diagnosis of facial paralysis (Bell's palsy) is usually certain. However, it is well to be aware of the fact that if the palsy has developed slowly, an intracranial neoplasm, especially pontine glioma, is likely

The prognosis is based on the severity of the lesion. Rarely will regeneration fail and the facial muscles atrophy. When regeneration fails, there is extreme relaxation of the tissues, and an unsightly deformity ensues

Guillain-Barré Syndrome *(Polyneuritis With Facial Diplegia). The cause of* the Guillain-Barré syndrome is unknown. An infective agent is not proved

There are no specific pathologic observations. Polyneuritis and degeneration of nerve roots may be found, with occasional changes in the cord.

The syndrome is characterized by symmetric flaccid paralysis with abolition of the tendon reflexes and with subjective sensory symptoms without objective change The patients are afebrile but may have had an antecedent febrile illness. All show a symmetric flaccid paralysis involving particularly the proximal muscles of the limbs and extending in severe forms to the cranial nerves, with a predilection for the seventh nerve Facial paralysis exists but involvement of the other facial nerves is unusual Increase in the protein content of the cerebrospinal fluid occurs frequently but is not a pathognomonic sign Differentiation from poliomyelitis is important and not difficult.

Tumors of Peripheral Nerves. *Neurofibromatosis of Recklinghausen.* The disseminated neurofibromatosis of Recklinghausen is characterized by multiple tumors arising from the sheaths of the spinal or cranial nerves, by cutaneous pigmentation and tumor formation, by abnormalities in the bones and frequently by evidences of defective development and other malformations.

The disease recurs in successive generations of affected families and therefore is believed to be the expression of an abnormal germ plasm The tumors of the nerve trunks are true connective tissue growths When there are intracranial neurofibromas, there may be meningeal growths, usually termed dural endotheliomas Gliomas and areas of gliosis often occur in association with neurofibromatosis of the generalized type In a large percentage of all cases of glioma of the optic chiasm there is associated Recklinghausen's disease. At the age of puberty the tumors become somewhat more numerous and larger than they have been previously The cutaneous lesions are usually symptomless.

Examination reveals irregular areas of yellow or brown pigmentation on the skin Interspersed in the areas between these large spots are small, circular, brownish areas resembling freckles. The skin is often dark. Numerous cutaneous tumors (molluscum fibrosum) of all sizes occur, ranging from 1 mm in diameter to tumors measuring 2 to 3 cm in size These cutaneous tumors are pigmented, soft or firm, and a few are pedunculated

Neurofibromas occur on both the cranial and the spinal nerve roots In some instances they seem to be confined to the two eighth nerves In others, many tumors are found in the cranium The vagus nerve is most frequently affected, and the fifth nerve stands next in frequency At times the brain stem and cerebellum are compressed by large neurofibromas

Tumors occurring on the spinal nerve roots give rise to signs of compression of the spinal cord or cauda equina They cannot be recognized as neurofibroma before operation even though cutaneous tumors are present It is unusual to find intracranial growths in the presence of pronounced cutaneous lesions

Plexiform neuromas extending diffusely through the tissues may occur over the cranium, causing elephantiasis of the scalp Plexiform neuroma may occur in the eyelid, orbit, sella, in the bones of the skull and in the arm or leg.

those muscles during activity. Tingling and numbness in the feet and toes are often present. These symptoms may or may not be associated with other indications of chronic alcoholism, for instance, looseness of the bowels, morning nausea, loss of appetite, tremor of the hands and rapidity of the pulse and flushed cheeks Gradually weakness of the legs and subjective sensory symptoms become more prominent and an altered mental state (polyneuritic psychosis or Korsakoff's psychosis) ensues. The memory is so bad that the names even of familiar objects are forgotten; there may be disorientation as to place and time. The patient may indulge freely in fictitious reminiscences.

Examination in the initial stage reveals marked tenderness to pressure of the plantar and calf muscles. The knee jerks may still be present but the ankle jerks are absent. There is cutaneous hyperesthesia, a moderate degree of sensory impairment (pain, touch, temperature, vibration) and postural modes of sensibility over the feet and toes Sensory loss spreads up the limbs and impairs postural sensibility so that the ambulant patient is likely to be ataxic and to sway when in the Romberg position.

In the advanced stages of the disease there is great loss of power in the distal segments of the limbs Often there is drop foot manifested by a high-stepping gait, but less often wristdrop. Paralysis progresses and complete invalidism may ensue. The muscles shorten, and contractures and deformities develop. The cutaneous hyperesthesia may make all handling of the limbs painful and difficult

Arsenical neuritis very closely resembles alcoholic neuritis even in the occasional presence of the polyneuritic psychosis This disease is exceedingly rare since the decrease in the employment of arsenical therapy

Neuritis of the Facial Nerve (Bell's Palsy) Bell's palsy follows an infectious interstitial neuritis or it results from exposure to cold There is a hemorrhagic interstitial neuritis involving that part of the nerve which lies in the temporal bone in close relation to the middle ear

In Bell's palsy resulting from interstitial neuritis there is pain, localized usually in the ear, extending into the cheek or into the occiput In Bell's palsy resulting from chilling, the palsy precedes the pain

Variations in symptomatology depend on the site of the lesion. If the lesion is distal to the point at which the chorda tympani separates from the seventh nerve, taste is not affected Involvement of the geniculate ganglion is accompanied by a herpetic eruption within the concha and external auditory canal. If the lesion is situated between the geniculate ganglion and the brain stem, there is no overflow of tears and the eye remains dry The presence of any one of these symptoms forces the assumption to be made that the lesion is probably situated inside the cranium and is not a simple Bell's palsy

On examination there is a hypotonicity of some and paralysis of other muscles of the face on the side of the paralyzed nerve The forehead and the cheek are smooth. The corner of the mouth sags The forehead cannot be wrinkled, the eye closed or the corner of the mouth retracted The patient cannot whistle Labial enunciation is affected. There is always an accumulation of food outside of the teeth on the affected side. Taste is lost over the anterior portions of the tongue. The lower lid falls away from the bulbar conjunctiva and tears run down the cheek, for the lacrimal punctum is no longer in position to collect them. Blinking of the eyelid is associated with twitching of the mouth

When the palsy is complete, the affected side of the face sags and the lip and cheek often become edematous. As a rule, the pain ceases within a few days

Within a few weeks examination reveals some return of muscle tone and later there is power of movement. The recovery is prompt and complete if the palsy is partial If paralysis has been complete, return of power is slow. The return of

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A benign neurofibroma rarely undergoes sarcomatous degeneration and metastasis.

The presence of cutaneous lesions or multiple subcutaneous nodules offers, as a rule, no difficulty in diagnosis since their nature is evident. In the central type of the disease the diagnosis cannot be made before operation. Roentgenograms of the bones may be helpful in diagnosis.

There is a *forme fruste of Recklinghausen's disease* characterized by the pigmented skin lesions without tumors

It is unusual to see a patient who is seriously disabled by this condition Intracranial or intraspinal tumors are serious since they are almost always so numerous that they cannot be removed.

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7

DISEASES OF THE ANORECTAL REGIONS AND GENITALIA

THE ANORECTAL REGIONS

THE PELVIC OUTLET

The topographic markings of the structures which limit the area within which the anus, rectum and the external genitalia are situated are known as the pelvic outlet The pelvic outlet is bounded anteriorly by the pubis, and laterally by the descending rami of the pubis and the ascending rami of the ischia. Posteriorly is the coccyx, and near its lateral limits are the spines of the ischia The greater and the lesser sacrosciatic ligaments form a diamond-shaped space which is divided into two triangles The anterior one is the urogenital and the posterior one is the anal triangle (Fig 7-1) These triangles may be visualized by passing an imaginary line

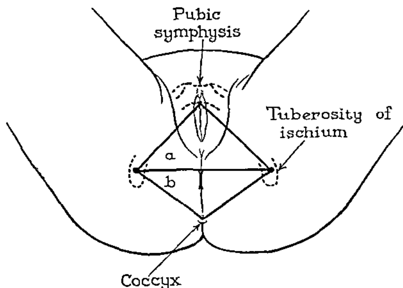


Fig 7-1 Pelvic outlet a, urogenital triangle. b, anal triangle

from the anterior portion of one ischial tuberosity to the opposite one Such a line passes about ½ inch (1 27 cm) anterior to the anus. This imaginary line passes through the dorsal portion of the central point of the perineum At the central point of the perineum the anteroposterior and transverse muscles meet. This point is sometimes designated the perineal body

THE PERINEUM

The Perineal Fascia and Muscles It is clinically important to remember that there are several layers of perineal fascia and muscles which may have implications in perineal infections and injuries. The first layer of the superficial fascia is continuous with the

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on the perineum anterior or lateral to the anal verge and the cyst often does not contain hair.

Unless complicated by infection, the condition is symptomless, although at times there may be slight discharge. Infection in due time is the rule. The symptoms then are those of superficial pain due to abscess, swelling, tenderness and fever In many cases there is a history of numerous acute episodes and surgical operations. Often relief follows simple incision.

A skin-lined orifice, or orifices, oval or round, situated in the midline over the sacrococcygeal region are usually indicative of pilonidal cyst or pilonidal disease. Such openings often, but not always, are hair-containing. In pilonidal cyst or sinus a probe passed through the orifice passes upward, whereas in a fistula-in-ano the probe will pass downward These sinuses and cysts tend to recur even after careful attempts have been made to remove them surgically

Hidradenitis Suppurativa. Hidradenitis suppurativa is a chronic inflammatory disease of the skin and subcutaneous tissue in those regions in which the apocrine sweat glands are situated; namely, the axillary, mammary, inguinal, genital and perianal regions This condition may resemble, according to Jackman, pilonidal disease.

The diagnosis of perianal manifestations of hidradenitis suppurativa is usually not difficult if the examiner thinks of this disease when he encounters what appears to be extensive anal fistula or pilonidal disease with many sinuses. Examination with the patient under anesthesia may be necessary to distinguish pilonidal cysts or anal fistula from hidradenitis suppurativa

Dermoids and Teratomas. Dermoids and teratomas are often midline tumors *attached to the periosteum of the sacrum and lying between the sacrum and the* rectum. The presence of the tumor often is not suspected until the size of the mass gives symptoms of pressure or unless the tumor is discovered on routine examination The tumor may burst into the rectum, and the patient may give a history of expelling a tuft of hair and teeth Occasionally a tooth or a tuft of hair may be visualized on protoscopic examination The diagnosis can be established by biopsy if teeth or hair is not present

THE ANUS AND RECTUM

The anal canal extends from the rectum to the anus or its opening on the skin, a distance of 1 to 1½ inches (2 5 to 3 8 cm.) It begins at the level of the levator ani muscles and ends at the apex of the prostate gland, which is directly in front of it, and with the tip of the coccyx behind and a little above. With the body vertical the anal canal has its axis inclining upward and forward toward the bladder, as soon as the sphincter ani is passed, the axis of the rectum changes to upward and backward toward the hollow of the sacrum. In introducing a speculum it should always be inclined first anteriorly and then posteriorly Opposite the level of the levator ani the circular muscular fibers increase to form the internal sphincter This extends down the anal canal for a distance of approximately 1 inch (2 5 cm) and ends above the skin margin The external sphincter surrounds the lower part of the canal and stretches in a spindle shape from the tip of the coccyx to the central point or tendon of the perineum Anteriorly it blends with the fibers of the levator ani and the other muscles of the perineum It is a thick, powerful, voluntary muscle and extends outward to the mucocutaneous junction.

Mucous Membrane The upper half of the mucous membrane of the anal canal has six or eight longitudinal ridges or folds (*columns of Morgagni*). Between the lower ends of these columns are small hollows called the crypts (of Morgagni), and the free edges

the anal canal The superior and inferior valves spring from the left posterior quadrant a short distance above and below the middle valve. At the juncture of the rectum and

surrounding parts and the dartos muscle The second layer of the *superficial fascia* (Colles' fascia), a fibrous underlayer, is continuous with the scrotum and passes forward to form the subcutaneous (Buck's) fascia of the penis, covers the spermatic cord, and is continuous with the deep layer of the superficial fascia of the abdomen (Scarpa's fascia). The anterior layer of the triangular ligament blends with the posterior layer of the deep superficial fascia. The deep layer of the triangular fascia is a continuation downward of the pelvic fascia, the obturator fascia, and passes onto the levator ani muscles and closes the gap between these muscles.

The superficial perineal space is situated between the crura of the penis covered by the ischiocavernosus muscles

The deep perineal space lies between the layers of the triangular ligament and contains the compressor urethrae muscle embedded in which is Cowper's gland with its duct which empties into the bulbous urethra

Extravasations of urine or blood in moderate amounts occur from injuries to the *penis anterior to the triangular ligament and thus pass into the superficial space and* are confined there Since this space extends forward and is continuous over the scrotum, the extravasating fluid passes forward and distends the scrotum In greater extravasations the urine may extend to the penis and along the spermatic cord, over the crest of the pubis to the surface of the anterior abdominal wall and laterally to the flanks but not down the thighs.

When rupture of the membranous urethra occurs, urine or blood may pass between the layers of the triangular ligament and be present in the superficial tissues anterior to this ligament. In more serious rupture urine escapes into the deep perineal space and thence back between the prostate and rectum or thence anteriorly behind the symphysis pubis into the perivesical space between the peritoneum and transversalis fascia

The Ischiorectal Fossa The ischiorectal fossa is situated between the tuberosity of the ischium and the anus Its main affections are from abscesses from the rectum. *It has* an anterior process which runs forward between the prostate gland internally and the ischiopubic ramus externally The posterior process is its deepest extension and communicates from side to side between the coccygeal attachment of the external sphincter muscle of the anus The ischiorectal fossa is enclosed by the levator ani and coccygeus muscles on the inward side and by the obturator internus muscle on the outward side.

Development of the Organs Incident to the Formation of the Perineum The bladder is first recognizable at a stage when it receives on each side a *mesonephritic duct* and a ureter Soon the four ducts, namely, the two ducts of the mesonephron and the two ureters, become separated and the ureters move laterally. The bladder when it begins to form is tubular in shape, then it expands and is saccular in shape with the elongate urachus at its apex The urachus is continuous with the umbilicus and may in rare instances maintain this connection between the umbilicus and the bladder throughout life

The female urethra is formed by an elongation of the original connection between *the primitive bladder and the urogenital sinus* T[illegible] counterpart of the female organ and in addition the pelvic portion [illegible] the prostatic and membranous urethra The [illegible] cavernous urethra

The prostate gland originates from multiple outgrowths of the urethral epithelium The outgrowths are soon surrounded by connective tissue and smooth muscle fibers The Skene glands in the female are homologous to the prostate but are few in number and situated near the external urethral outlet

The bulbourethral glands (Cowper) of the cavernous urethra of the male are homologous to the vestibular glands (Bartholin) of the female.

The seminal vesicles arise as outpouches from the mesonephron and gain muscular walls from the mesenchyme. There is no homologous organ in the female.

Pilonidal Cyst and Sinus. Outside of the pelvic outlet in the midline of the coccygeal region, if there has been a failure of union of the ectodermic layer of the embryo, there occurs below the surface an inclusion of hair-growing tissue termed pilonidal cyst. However, as N. D. Smith has pointed out, this cyst may be situated

ectoderm is on or near the surface of the body. Surface structures have as an important function the protection of the organism from the adversities of the environment, and at least a part of this protection is obtained through the ability to perceive pain. Structures arising from the mesoderm and entoderm when stimulated do not give rise to definite localized pain A sharp pain in anorectal disease points to a pathologic condition involving the anus

Imperforation and Associated Malformations. Imperforation and the malformations associated with imperforation constitute most of the congenital disorders of the rectum. The various types of imperforations may be enumerated as the imperforations of the rectum with vesical, posterior urethral, uterine or vaginal outlet. In an occasional instance there may be a spinal outlet In females the genital outlets may open into the rectum Also the rectum may be imperforate for lack of an anal outlet, or the rectum may have difficulty in emptying, owing to stenosis of the anus and thus may empty through the vagina.

IMPERFORATE RECTUM The rectum may be absent, or its descent may be arrested at any point distal to the promontory of the sacrum The usual point of arrest is at the peritoneal reflection A fibrous cord may extend from the apex of the rectum to the anal cul-de-sac or from the imperforate rectum to the bladder or the urethra

The first symptom of an imperforate rectum after birth is absence of bowel motions. This is followed by the symptoms of obstruction of the colon

On examination there may be a normal-appearing anus and anal canal, or the anus may be absent. If the anal canal is present, the well-lubricated little finger when inserted into the rectum reveals a shallow rectum completely occluded

Imperforate rectum with vesical outlet is a rare condition. The communicating passage is narrow and lined with mucosa. It opens into the bladder, often near the trigone The diagnostic symptom is fecal (meconium-stained) urine On examination the finger is stopped at a shallow depth It is then obvious that the source of the feces-stained urine is an opening of the rectum into the urinary system. Communications other than from the rectum to the bladder are usually in the posterior urethra

In *imperforate rectum with posterior urethral outlet* the passage from the imperforate rectum may open into the prostatic or membranous urethra. Some of the patients who have this malformation attain adult life The diagnosis of imperforate rectum with vesical outlet or urethral outlet is definitely established by endoscopic examination

In *imperforate rectum with vaginal or uterine outlet* the communication usually opens into the vestibule of the vagina. The symptoms and signs are the same as those of an imperforate rectum, with the addition of the passage of feces from the vagina Often these openings may be adequate for drainage of the rectum, and consequently the patients may reach adult life The diagnosis is made by digital or endoscopic examinations once the condition is suspected.

Imperforate rectum with spinal outlet is an obstetric curiosity. These babies do not usually survive

In those who have a *urogenital outlet in the rectum,* the vagina may be normally formed but opens into the rectum, and in some cases the abnormality is unnoticed until the menstrual flow is established The bladder is absent and the ureteral orifices may be at the peritoneal reflection in the rectum. Urine in the rectum is usually well tolerated without an ascending urinary infection. The diagnosis is made by endoscopic [illegible]

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the sigmoid flexure there is another fold on the anterior wall which tends to obstruct the view when examinations are made. These valves are composed of connective tissue and circular muscular fibers covered with mucous membrane.

The combined length of anal and rectal canal is 4 to 5 inches (10.2 to 12.7 cm.).

RECTAL EXAMINATION. The finger can palpate the anal canal and rectum for a distance of 4 inches (10.2 cm) from the surface. Anteriorly, in men, as soon as the finger passes the sphincters, the apex of the prostate can be felt, also the membranous urethra, particularly if it contains a bougie or sound. The prostate can be outlined and its size determined. If the prostate is not enlarged, the base of the bladder above can be palpated and the tip of the finger will reach the rectovesical pouch From the upper or posterior edge of the prostate and extending from near the midline upward and outward, are the seminal vesicles. Just to the outer side of the upper end of the seminal vesicles are the lower ends of the ureters Posteriorly the coccyx and the hollow of the sacrum can be felt Laterally the finger can explore the region of the spine of the ischium, the sacrosciatic foramina, and the tuberosities

Ataxic Sphincter This is a condition in which the external sphincter lacks tone, owing to degenerative changes in the posterior nerve roots and posterior columns of the spinal cord, often as a result of tabes dorsalis or of syringomyelia The anus appears normal on inspection, but when it is separated, it remains partly open instead of closing instantly as it does normally, and then very slowly resumes its usual state of contraction When tabes dorsalis is not otherwise suspected, this symptom often gives the first indication of the disease

In some patients an ataxic sphincter, in the absence of any demonstrable lesion of the peripheral nerves or the central nervous system, is due to a prolonged use of laxatives

Rectal Shelf Masses Properly the term rectal shelf has been employed to designate that condition in which a palpable mass impinging on or attached to the anterior rectal wall causes a ledge or shelf to be felt Such a mass deserves serious evaluation because it may call attention to a lesion remote from the rectum. The mass may resemble a primary carcinoma of the rectum and thus lead to an error in diagnosis and prognosis. A patient may consult a physician because of symptoms produced by the rectal shelf or a pararectal mass without relating these symptoms to any which result from the primary lesion, or the reverse situation may be encountered The commonest causes of pararectal masses among women are lesions of the genital system, and among men lesions of the gastrointestinal tract and the stomach (carcinoma) in particular

Congenital Malformations of the Anus and Rectum. ***Persistence of Cloacal Duct.*** In persistence of the cloacal duct there is a narrow outlet from the rectum to the raphe of the perineum, scrotum, underside of penis, prostatic urethra or bladder In the female the opening may be along the perineal raphe or into the vestibule of the vagina

The rectum develops from the entoderm and the mesoderm, the anus, the proctodeum, develops as an invagination of the ectoderm The primitive rectum and the primitive anus gradually approach each other Absorption of the epithelial layers of the proctodeum and the primitive rectum permits the joining of the lumina

The conjunction of the rectum and the anus, at a point in front of the posterior end of the gut, leaves a cul-de-sac This cul-de-sac and the connecting canal are largely absorbed during fetal life Imperfect absorption is the cause of a congenital posterior rectocele. The region where this posterior cul-de-sac and the communicating canal are situated is a favorite site for the occurrence of dermoid cysts and other teratoid tumors of the rectococcygeal space.

As has been indicated, the anus and the rectum developmentally and functionally are distinct organs, arising from different layers of the embryo, and thus are subject to diseases inherent to the tissues from which they arise. The diseases of each organ present symptoms which are unlike those of diseases of the other. This is particularly true of ... of pain. The anus arises from ectoderm Any structure which arises from

hemorrhoids and polyps Some large papillae may be drawn out of the anus by the palpating finger. Attempts to pull these away with the examining fingers cause acute pain and hemorrhage

Abscesses and Ulcers. *Anorectal Abscesses.* The diseases such as fissures, ulcers, abscesses, fistulas and abrasions are often initiated by breaks in the continuity of the anorectal lining membranes resulting from trauma and not by direct invasions of the tissue by bacteria, viruses or parasites.

An anorectal or a rectal abscess develops from an injury made by the passage of formed feces of large caliber, often containing hard pellets which tear one or more of the anal crypts. These tears are common and usually heal promptly. Occasionally such a tear does not heal promptly, and then an inflammation of the crypt occurs, spreads to the surrounding tissues, and results first in the condition known as cryptitis The cryptitis either heals or proceeds to abscess formation.

The extent of the inflammation and the structures affected determine the type of anorectal abscess present. For instance, if the pus forms above the levator ani muscle, the abscess is either a *superior pelvirectal abscess* or a *retrorectal abscess,* depending on which of these spaces is occupied An abscess posterior to the levator ani muscle is an *ischiorectal abscess.*

The superior pelvirectal and retrorectal inflammations originate outside the rectum These inflammations are frequently extensions of an infection of the adjacent pelvic urogenital organs, or of the intestines Occasionally an ileitis may originate such an abscess

The studies by Hill and co-workers of structure of the anal glands offer a possible explanation of the spread of infection through these glands There is a wide individual variation as to number, depth of penetration and contour of the anal glands. Lack of complete canalization of the terminal portion of the anal glands was observed in 3 newborn infants. In some of the specimens from adults the cells lining the anal glands presented apical cytoplasmic vacuoles which stained positive for mucin

Various existing traumatic, bacterial and constitutional factors unite to permit infection to spread by way of the anal glandular system The extension of anal glands upward beyond the anorectal line into the rectal submucosa offers an explanation of the occasional occurrence of abscess and fistula in this region. The deep penetration of an anal gland extending into the internal sphincter points to possible avenues of invasion along muscle bundles, fascial planes and adjacent structures to these lines of cleavage A definite glandular cyst in an adult supports the claim that abscess and fistula may develop without communication with the anal canal

Symptoms In the superior pelvirectal and retrorectal abscesses pain is deep but not intense Prostration is often profound, for large quantities of pus can accumulate in these spaces There may be intermittent fever. These abscesses are often the cause of the so-called pyrexia of unknown origin In a few who have these abscesses the temperature may be as high as 105 F (40.5 C) or more.

If the abscess has had its origin in a pelvic organ, for instance, an ulcerative colitis, or from an ileitis, or if it has originated in the prostate and extended, the whole side of the buttocks may become exceedingly tender, reddened and swollen. There often are fever and an accompanying diarrhea.

An abscess arising in the anus which extends to the perianal tissues is characterized by local redness, swelling, pain and hot skin similar to the manifestations of a superficial abscess elsewhere

Examination. On examination the anal orifice and buttocks often appear normal On digital examination of the rectum above the anorectal line, a soft tender mass may be palpated The leukocytes vary in number from normal to 30,000 per cubic millimeter of blood.

The anus may be completely formed, but occluded at the anorectal line by a thin, elastic diaphragm of fibrous or mucocutaneous tissue due to the persistence of the anorectal membrane. In these infants there are no bowel motions. Examination often reveals an impulse or a fluctuation of the distended rectum.

The diagnosis of imperforate anus is usually made by inspection and palpation

CONGENITAL STENOSIS OF ANUS The normal anus of an infant should admit without difficulty the lubricated little finger. The canal may be narrow throughout or segmentally. The narrowing may be so slight that the passage of soft feces causes no difficulty, but harder masses give rise to constipation and straining

The diagnosis is made by digital examination. Normally the anal canal varies in caliber, and due allowances are given for these normal variations.

Anal Ulcers (Fissures). Anal fissures and ulcers are usually manifested in the third, fourth and fifth decades Occasionally they are present in children, but rarely in the aged Two men have anal fissures or ulcers to each woman so affected Nine of every 10 anal ulcers or fissures occur in the posterior portion of the canal.

Anal fissures or ulcers are almost always caused by fecal trauma However, trauma also may result from sharp particulate matter or a fishbone in the feces A common source of anal trauma is the introduction of a syringe tip An uncommon source, but nevertheless one that does occur, is sodomy. Sodomy may be followed by gonorrheal proctitis and ulcers Injury and destruction of an anal crypt may result in ulceration

The characteristic symptoms are bleeding with bowel motions, and pain occurring from a few minutes to a half hour after bowel movement The pain continues for variable lengths of time and then entirely or partially subsides until the next bowel movement There is a wide variation in the degree of pain. Some patients may have little or no pain from an anal ulcer or fissure

On digital examination the anus is exceedingly tender When the sphincter is spread open, the ulcer is seen to be oval or circular and just within the grasp of the muscle Often it has a superficial fistulous tract leading toward the skin surface and the teatlike process known as the sentinel pile at the skin margin of the ulcer.

A chancre of the anus may closely resemble the usual type of anal ulcer Anal chancres occur more frequently in women than in men

Cryptitis. The anal crypts are small pockets distributed about the anorectal line Inflammation of these pockets is termed cryptitis This inflammation has been designated infected hemorrhoids.

The anal crypts have their openings directed inward They are subjected to trauma by the passing feces Following trauma, mucosal abrasions within the crypts may originate an inflammatory reaction. These reactions often terminate in pararectal abscess.

The symptoms of cryptitis closely resemble those of ulcer or fissure There is pain, commencing after a bowel movement Pains referred to the perineum, the urogenital region, the sacrum and coccyx, or down the legs are common On examination there is tenderness along the anorectal line

Cryptitis is not usually an inflammation of a single crypt, but an inflammatory reaction that has originated in a crypt and then spread along the anorectal line. The proctoscopic findings are characteristic enough for diagnosis by an experienced examiner

Papillitis. Papillitis is an inflammation of the anal papillae The anal papillae are often found to be hypertrophied. This enlargement without symptoms is considered to be an incidental condition.

Enlarged papillae may be torn by the stool, resulting in sharp pain in the anus and bleeding Usually there are no symptoms of papillitis.

On rectal palpation the finger may perceive soft or firm, teatlike projections at the anorectal line. Large papillae may cause some examiners to suspect internal

is differentiated from perianal tuberculosis by biopsy. Usually, however, the diagnostician has little doubt of the differentiation even without laboratory aid.

The prognosis is never good. The condition usually is secondary to tuberculosis in some other part of the body, and even when the ulcers heal, there is a constant danger of reinfection Often, too, the disease advances despite all treatment

Tuberculosis of the Rectum. Tuberculosis of the rectum practically always is secondary to an infection elsewhere in the body, the lungs being the usual primary seat. The rectum is involved more rarely than the intestinal regions above but more frequently than the anus

Three forms of rectal tuberculosis are described: the miliary, the ulcerative and the hyperplastic

Miliary tuberculosis of the rectum is rare and always is part of a generalized tuberculosis Multiple tubercles form beneath the mucosa and these coalesce and slough to form irregular ulcers Sometimes these ulcers will burrow beneath the mucosa to form small fistulas.

In *tuberculous ulceration* of the rectum the tubercle bacilli are carried to the rectal mucosa through the lymphatics and there form tubercles As these break down and coalesce, they form small ulcers The edges of these ulcers undergo a progressive degeneration which leads to a constant increase in their size until there are large ulcerations.

Secondary infection of the ulcers may cause them to perforate the musculature of the rectum and even of the peritoneum, resulting in tuberculous abscesses of the perirectal tissues and subsequent fistulas which may extend into the bladder or other contiguous organs with the production of a tuberculous peritonitis

The symptoms of tuberculous ulceration of the rectum are cramplike pains during bowel movements, often accompanied by tenesmus, and frequent stools, sometimes numbering as many as 30 during the 24 hours Contained with the stool is a mucopurulent, blood-tinged, fetid discharge The discharge, scanty in the beginning, increases in quantity until it becomes profuse. When the discharge is copious, it is thin and irritating to the anal skin

On examination the ulcers are irregular, gray, and rough-appearing with slightly thickened, irregular and undermined edges The mucosa between the ulcers is likely to be inflamed and edematous

The diagnosis of the disease is based on identification of the tubercle bacilli by cultural means, guinea pig inoculation and on the characteristic appearance of the ulcers and the fact that the disease occurs in a patient who has active pulmonary tuberculosis or tuberculosis of some other part of the body

Hyperplastic tuberculosis of the rectum is a rare form of the disease It is characterized by a localizing thickening of the intestinal wall due to a round cell infiltration and the massive deposit of fibrous tissue This condition, commonly known as tuberculoma, may resemble malignant disease. The treatment is surgical

Tuberculous Pararectal Abscess. The tuberculous pararectal abscess has an insidious onset. When it has fully developed, there is no pain or tenderness over the infected region Usually the only symptom will be distortion of the part from the accumulation of pus The condition always is secondary to tuberculosis in some other part of the body, usually the lungs, and it may occur during the course of a tuberculous ulceration of the rectum An accumulation of fluid beneath the skin of the buttocks and near the anal margin, without acute symptoms, arouses suspicion of a tuberculous abscess, particularly in a person who has pulmonary tuberculosis

Tuberculous Fistulas. These fistulas result from the evacuation of pus from a tuberculous abscess The fistulas may connect with the skin of the buttocks or with any organ adjacent to the rectum and anus.

Syphilis. There may be itching early, but the chancre or ulcer is painless unless it is within the grasp of the sphincter or is complicated by a mixed infection.

When the abscess has extended to involve the perianal tissues, particularly in the presence of an ileitis or chronic ulcerative colitis, there may be swelling and redness of the skin and induration of the tissues of one side of the buttocks. When these manifestations are present, rectal examinations may be impossible because of the tenderness and pain.

The superficial abscess can be recognized from the mildness of its manifestations. Rectal examinations are painful but usually can be performed if care is exercised during the examination. In the presence of the superficial abscess, the inside of the rectum feels normal and it is not tender

DIAGNOSIS The diagnosis of an acute, superficial abscess is made from the presence of pain, tenderness and redness of the affected parts Fluctuation may be present

The diagnosis of deep abscess such as pelvirectal and retrorectal abscesses may be uncertain The prostration, high fever and leukocytosis, and often the sensation of weight and heaviness in the pelvis, draw attention to this region. These symptoms accompanied by the presence of a tender rectal mass justify a presumptive diagnosis In due time, after exercise of judgment and caution, an exploratory incision may be required for both diagnosis and proper treatment

Anorectal Tuberculosis. A tuberculous infection of the rectum and adjacent tissues occurs in a patient who has swallowed infected milk or sputum, and thus an opportunity has been rendered the bacillus to invade the tissues of the rectum The tubercle bacillus may invade the anorectal regions from an anorectal focus through the lymphatics, through the blood stream and by direct extension from contiguous organs from inside the pelvis

Tuberculosis of the Anus. *Tuberculosis of the perianal skin* occurs as lesions, miliary, ulcerative, lupoid and papillary (verrucous) The lupoid and papillary forms are rarely observed

Miliary lesions of the anus are a part of an advanced and generalized infection in some other part of the body Multiple minute nodules form beneath the epidermis and gradually coalesce and break down to become the ulcerative type of tuberculosis. Diagnosis is established by biopsy and guinea pig inoculation The prognosis is poor

Ulcerative tuberculosis of the anus is the commonest form of the disease It may be secondary to a focus in the lungs or intestines but is more likely to be a primary infection than is tuberculosis of the rectum Small nodules form in the skin and then coalesce and disintegrate to become ulcerations The ulcerations may be single or multiple, and at times are epitomized by massive ulceration that involves the entire perianal region The individual ulcers usually are superficial but may involve all of the layers of the skin. Their shape is irregular and they have a distinct margin depressed below the surface of the raised base Sloughing and undermined edges are characteristic

Patients who have severe exudative and destructive pulmonary disease are more subject to anal fistulas than patients who have the productive type of the disease. The perianal abscess either precedes, or concurs with, a progressive or regressive modification of the pulmonary process Patients who have severe tuberculosis may exhibit multiple anal fistulas surrounded by granulation tissue, extensive zones of infiltration and detachment of skin at the external openings, whereas in the fibrous type of pulmonary tuberculosis the fistulas are benign When ulcerative pulmonary tuberculosis exists, specimens obtained by scraping the fistulous tract often yield tubercle bacilli In the fibrous type of pulmonary tuberculosis with negative sputum positive results are less frequent Tissues surrounding anal fistula often yield positive evidence of tuberculosis. The anatomic and clinical observations indicate that the perianal tuberculous abscess is probably of hematogenous origin

The diagnosis is established by biopsy and guinea pig inoculation Epithelioma

opening but no external opening. Many variations of these fistulas exist (Fig. 7-2). Often there are multiple external openings which communicate with each other and with an internal opening.

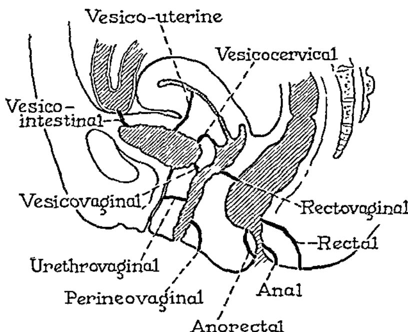


Fig 7-2. Common sites for anal, anorectal, rectovaginal, vesicocervical, vesicouterine, perineovaginal and urethrovaginal fistulas

The genesis of fistula is a pyogenic organism with the formation of an abscess. The organism present is usually the staphylococcus, not the tubercle bacillus.

Inflammation of the crypts of Morgagni extending to the perirectal tissue may terminate in formation of abscess The abscess may rupture into a pelvic organ or through the skin of the buttocks and thus establish a fistula An abscess of this type may rupture into the vagina, the uterus, the urethra, the prostate gland or the bladder. The external opening of these fistulas does not bear a constant relationship to the position of the internal opening There may be many external openings over both buttocks and thighs

SYMPTOMS Fistulization about the anus and rectum is characteristically secondary to the rupture of an acute abscess somewhere about the rectum or the genitalia. The symptoms of the abscess are obtained from the history and are often summarized by the presence of pain, redness, swelling and fever. The abscess opened spontaneously or was lanced, and relief from symptoms followed the drainage After the rupture or lancing of the abscess a small opening persisted in the buttocks from which there was constant oozing of a purulent or serous discharge which in time ceased After a lapse of time another acute abscess developed This sequence of events may be repeated with the maintenance of a single fistula; or, with formation of each new abscess, new fistulas may be added until the entire buttocks and perirectal tissues are involved in fistulas.

EXAMINATION On examination the external opening of the fistula is readily found Often a probe may be gently worked through the fistulous tract until it emerges through the internal opening in the rectum under direct visualization through an endoscope. Often, however, the tract is tortuous and it is impossible to work the probe through the tract in an unanesthetized or, on occasion, an anesthetized patient. The probable internal opening may be discovered by palpating with the finger from within the rectum.

If the lesion is single and fairly characteristic of chancre, a presumptive diagnosis can be made A definite diagnosis depends on positive results of darkfield examination. Serologic reactions of the blood are seldom positive before the second week or later.

Condyloma Latum. This is a secondary manifestation of syphilis occurring within the anus or in the perianal skin and characterized by wartlike elevations occurring singly or in groups.

A pearly white, flat, oval or rounded patch begins on the skin surface and multiplies These plaques have a tendency to form large fungating masses which may encircle the anus and extend to the vulva or to the scrotum The masses are broad, flat, warty elevations with sharply defined edges which rise at right angles from the skin The surface is flat and covered with a glistening, grayish necrotic membrane Diagnosis depends on a positive Wassermann reaction, combined with the history of a primary lesion and the presence of the wartlike plaques just described

Rectal Injuries and Foreign Bodies. ***Rectal Injuries.*** Spontaneous rupture of the rectum may occur as the result of crushing blows to the abdomen or pelvis, and from accidental dilatation from the nozzle of a pneumatic hose entering the rectum Many different sorts of anorectal injuries are sustained in farm accidents; for instance, *falling astride a fence post, and falling on the handle of a pitchfork.*

The symptoms are severe abdominal pain, prostration, shock and hemorrhage. Diagnosis is not difficult, as a rule, and should be made early so that surgical intervention may be performed immediately to prevent or to alleviate peritonitis

Foreign Bodies. Foreign bodies find lodgment in the rectum usually by being *swallowed, but they may be inserted through the anus In those who have mental* diseases all manner of objects may be packed in the rectum Rarely, they may gain entrance from a contiguous organ or they may form within the intestinal tract (gallstones, fecaliths)

Symptoms are extremely variable and depend to a great extent on the size and shape of the object within the rectum. Small objects, such as fishbones, which become caught within the anus cause a sudden, sharp and constant pain

The diagnosis depends entirely on rectal examination. Endoscopic and roentgenologic examination should be resorted to whenever rectal examination leaves the least doubt as to the nature, extent or situation of the offending body.

Anal Stenosis and Contracted Anus (Pectenosis and Anal Fibrosis) The inflammatory stricture follows extensive removal of the anal skin, and superimposed infection may result from (1) hemorrhoidectomy, (2) trauma, (3) the injections in the treatment of pruritus and hemorrhoids, (4) the excision of fistulas and anal condylomas, (5) chronic ulcerative colitis, (6) lymphopathia venereum and (7) irradiation therapy The stricture often is tubular and may be from 1 inch to 3 or 4 inches (2 5 cm to 7 6 or 10 2 cm) in length, and the strictured lumen may be measured in millimeters

Bowel movements are difficult and painful In some cases blood and pus are passed from the rectum with stool, or sometimes as a leakage, independently of bowel movement

The anus and rectum are of small caliber and very tender, so that digital examination may be impossible Often a proctologist can pass an instrument of small caliber for endoscopic examination of a patient who cannot permit a digital examination.

The diagnosis is evident from the foregoing findings. The treatment is *dilatation* except in those who have chronic ulcerative colitis, active lymphopathia venereum or irradiation therapy

Anorectal Fistula. A *complete anorectal fistula* implies an internal opening in the anus or rectum or at the anorectal line, and an external opening in the skin surface near the anal orifice or in the buttocks. An *incomplete fistula* has an internal

On inspection and palpation there is a livid, firm, tender swelling beneath the smooth, shiny skin After the acute symptoms have subsided, the swelling will seem shotlike, a characteristic that will persist for a long period There are sometimes erosion of the overlying skin and bleeding from the thrombotic hemorrhoids. A swelling on one side of the anus which is tender and painful, firm and livid, beneath smooth, shiny skin is diagnostic.

Internal Hemorrhoids. The etiologic factors capable of producing internal hemorrhoids are heavy lifting, standing posture, sedentary habits, heredity, portal hypertension, constipation, straining at stool, and infection A low-grade, long-standing infection weakens the venules and veins of the rectum so that the weakened lining of the veins ruptures and acute thrombosis results After repeated thromboses occur, there is prolapse which is constant, and after bowel movements the prolapsing mass is replaced regularly with attendant trauma. The prolapsing mass increases in size and protrudes through the sphincter muscle The muscle may lose its tone, owing to continued pressure and long-standing disease.

Without thrombosis internal hemorrhoids are painless. Bleeding occurs at bowel movements Blood may squirt in a small stream as the patient strains The quantity of blood lost at any bowel motion is seldom great, but the staining of the water in the bowl may give the impression of a large hemorrhage Internal hemorrhoids will occasionally bleed spontaneously, for instance, while the patient is pursuing the daily tasks.

A prolapse of the mucous membranes may occur at bowel motion The prolapsing mass often retracts without assistance When the prolapse is marked, however, the mass will not return within the lumen of the rectum and must be replaced by the patient A prolapse hemorrhoid which remains outside the anal canal will cause a constant dragging pain in the rectum, and there may be perianal edema.

The examining finger can feel large internal piles or sclerosed piles but not small ones The diagnosis is made by proctosigmoidoscopic examination.

PROLAPSED INTERNAL HEMORRHOIDS. Prolapsed internal hemorrhoids may get caught in the grasp of the anal sphincter and become edematous. To replace prolapsed hemorrhoids, ask the patient to lie on the left side Bathe the hemorrhoids with cold water to reduce the edema Apply petroleum jelly liberally with cotton Exert pressure on the protrusion with one hand while the other hand is easing the constriction of the edematous folds of the anus. If the edema is so great that the hemorrhoids cannot be returned, it may be necessary to anesthetize the sphincter with some local anesthetic agent

If the hemorrhoidal mass cannot be thus replaced, the condition is termed strangulated piles or hemorrhoids This condition requires hospitalization and appropriate treatment

Proctitis and Proctosigmoiditis. Proctitis is an inflammation of the rectum. Sigmoiditis is an inflammation of the sigmoid flexure, that portion of the colon which extends from the crest of the ilium to the level of the third sacral vertebra Inflammation of both the rectum and sigmoid is known as proctosigmoiditis

Proctitis or proctosigmoiditis may result from constitutional disorders such as diarrhea and fever caused by the exanthems, influenza and hepatic diseases Any chronic disease accompanied by diarrhea may cause proctosigmoiditis. All of the acute infectious dysenterial diseases are accompanied by proctosigmoiditis.

The manifestations are often those of hemorrhoids, the hemorrhoidal irritation having been produced by tenesmus and the frequent passage of watery bowel motions which may contain blood and mucus.

Diagnosis is established by the presence, on endoscopic examination, of a reddened, inflamed mucous membrane of the rectum and rectosigmoid. Time and repeated observations may be necessary to be sure that the disorder is not an early stage of chronic ulcerative colitis

DIAGNOSIS. The diagnosis is made from the findings revealed by physical and endoscopic examinations.

Hemorrhoids. Hemorrhoids appear exter... ternal hem... belo ...

...from the superior hemor-

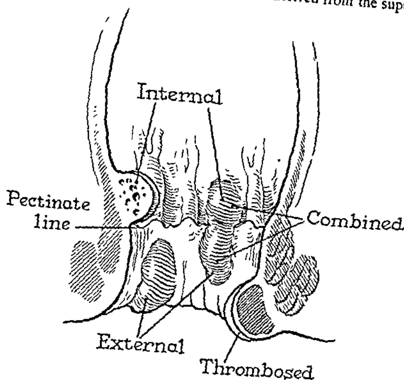


Fig 7-3 Hemorrhoids

rhoidal vein and are situated above the anorectal line They are covered with mucosa

External Hemorrhoids. External hemorrhoids comprise skin tabs and varicosities of the anal veins Since man walks on his hind legs, the cause of external hem... ...present in four-footed animals. The incidence ... men and women ... objectionable because of the difficulty they cause in efficient cleansing of the parts. They usually do not produce symptoms

Varicosities are seen as bluish swellings just within the anal canal or at the anal margin and are soft and compressible

The foregoing described diagnostic findings are unmistakable and symptoms are usually absent

THROMBOTIC EXTERNAL HEMORRHOIDS Thrombosis of external hemorrhoids results from a strain or traumatism to the thin-walled anal veins Coughing, sneezing, lifting, or straining at stool may cause one or more of the coats of a diseased vein to give way, to be followed by formation of clot within the walls of the vessel or in the surrounding connective tissue Once the thrombus is formed, it may remain, and the swelling and pain gradually cease in from 3 to 10 days If rapid distention of the veins takes place, rupture may follow

Immediately following the rupture there is a feeling of continuous discomfort. Sometimes throbbing, burning pain in the anus ensues and continues. As the pain and soreness develop, it becomes more and more difficult to sit in comfort or to move the bowels. Pressure on the tumor is painful. The discomfort continues to be severe for 2 or 3 days and then gradually subsides.

[illegible] of more proximal segments of the bowel. These masses

Pruritus Ani [illegible] of nervous tension and irritability. The unusual causes of pruritus ani are diabetes, infestation with pinworms (see Diseases of the Colon, Chapter 13), pediculosis pubis, fungous or other infections of the skin, general dermatosis and infections of the anorectal region. A severe anal pruritus may result from the application of salve for the treatment of hemorrhoids.

Localized itching may be mild and present only occasionally, or it may be continuous and severe. The itch is more intense after the patient has retired for the night, or perhaps after he or she has been sleeping for half of the night The itch may be agonizing, and there is an overwhelming desire to scratch the affected area The patient scratches himself unconsciously when awake or during light sleep

Unbearable and constant itching, in time, because of the consequent loss of sleep and persistent irritability, will lead to physical fatigue and mental exhaustion

On examination, interspersed about the anus will be excoriations from scratching The skin about the anus is often reddened, swollen and either dry or moist In advanced severe pruritus ani the skin assumes a leathery appearance Lichenification, a pale and blanched appearance because of a loss of pigmentation, ensues. The radiating skin folds are likely to be edematous and hypertrophied, and the sulci between to become cracked or fissured

The diagnosis of pruritus ani depends on the history of itching about the anus and the findings revealed on physical examination

Tumors of the Anorectal Regions. ***Benign Tumor.*** *Verruca acuminatum of the anus* has the synonymous names anal wart, papilloma and verruca. Warts and papillomas that occur about the margin of the anus and within the anal canal are often called venereal warts Condyloma latum, however, is the only one of venereal origin

The papillomas consist of connective tissue and blood vessels covered with stratified epithelium They arise from hypertrophy of the papillae of the skin and are caused by irritating discharges such as occur in gonorrhea, hemorrhoids, proctitis and colitis. Verruca acuminatum is an excrescence which begins on one side of the anus and often spreads rapidly until it surrounds the anus as a large cauliflower-like tumor attached to the skin by many pedicles The growths are soft and pliable, of a pale pink color, and bleed freely when injured They are distinguished from epitheliomas by the absence of induration at the base or ulceration of the surface

Verruca acuminatum and papillomas are to be distinguished from the highly malignant papillomatous forms of anal epitheliomas which are situated at the anal verge or within the anal canal. Likewise they are differentiated from protruding hypertrophied anal papillae which may protrude from the anus. The diagnosis is established by biopsy and histologic study

Malignant Tumors. Anal Carcinoma (Epithelioma). Anal carcinoma arises from the squamous cell epithelium of the skin and mucocutaneous junction and thus *is an epidermoid carcinoma having all the characteristics of carcinoma of the skin* and of lesions of mucocutaneous junctions such as the lip or vulva Most of the growths are ulcerating lesions, but they may appear as cauliflower-like masses protruding from the anus

The complaint may be of anal discomfort, with or without relation to stool, and the passage of large quantities of fresh blood. In addition the patient may report the presence of a tag or growth within or near the anal orifice which has suddenly enlarged and become painful These features are highly suggestive of an anal lesion, and the odds are greatly in favor of anal fissure, since anal epithelioma occurs only rarely. Nevertheless the possibility of epithelioma must be considered in all middle aged patients of either sex

Gonorrhea. Gonorrhea of the rectum is uncommon. The gonococcus may gain entrance to the anus and rectum by inoculation of pus from an infected urethra, by pederasty or by the contamination of instruments. Diagnosis is made only on the basis of positive cultures.

Prolapse, Protrusion and Procidentia of the Rectum and Sigmoid Colon. Prolapse or procidentia is a descent of one portion of the rectum or anal canal into or through another In complete prolapse there is an intussusception of the rectum

Prolapse of the rectum is classified as *incomplete or partial prolapse* when only the mucous membrane is involved, and *complete prolapse or procidentia* when all of the coats of the bowel form a part of the prolapse When the colon becomes involved, the prolapse is termed a *colonic procidentia,* since the anus does not have three coats. A patient can have an anal prolapse but not an anal procidentia.

The common causes of prolapse and procidentia are either intrinsic or extrinsic to the bowel The intrinsic conditions causing prolapse and procidentia are hemorrhoids, polyps, neoplasms, foreign bodies and sodomy. Extrinsic conditions are parturition, tumors and displacements of the uterus, hypertrophy and tumors of the prostate, visceroptosis, intra-abdominal tumors, prolonged vomiting, coughing or crying, tightly applied belts and corsets, certain violent exercises, urethral calculus and urethral stricture, and phimosis.

Prolapse occurs in children less than 5 years of age and in the aged who have debilitating disease and nutritional disorders with a loss of ischiorectal fat.

Disease of the spinal cord resulting in paralysis or relaxation of the anal sphincter or levator ani muscle, such as tabes dorsalis, predisposes to prolapse and procidentia

In the beginning there is protrusion only at stool, a prolapse. At first the protrusion is of slight degree The protrusion may gradually become greater until several inches or more of the bowel may remain outside. Subsequently the external sphincter becomes more and more atonic until it becomes difficult or impossible to keep the bowel in its proper place. Often the condition is intermittent. Discomfort, described as a bearing-down sensation, is present whenever the mass is outside of the body, and it may be present at other times.

The mucosal prolapse is a redundancy of the mucosa, which protrudes through the anus at stool. It is bright red, moist and glistening, and has small hemorrhagic areas on its surface Protrusion through the anus occurs at stool and the protruded mass may return within the sphincter spontaneously or may remain outside until pushed within Protrusions which have been present for a long period may remain outside of the anus When this occurs, the reddened congested mucosa often becomes eroded and ulcerates With the passage of time the mucosa turns pale and assumes a leathery appearance and the sphincter loses its tone.

DIAGNOSIS. Prolapse of the rectum which does not extend beyond the anus is diagnosed by proctoscopic examination An abnormal looseness or wrinkled swelling of the mucosa will be seen and this may involve a segment of the rectum or its entire circumference

Procidentia recti, the displacement of the rectum with all of its coats into its lumen or through the anus, is distinguishable by the presence of the musculature, shown by concentric rings in the mass. These rings constitute the differential point from a prolapse protruding from the anus in which folds radiating from the anus are seen in the mass. The mucosa of the procidentia, after long exposure outside of the body, becomes thickened and firm.

A procidentia of the rectum which does not protrude from the body can be palpated with the finger and is felt as a mass, with a lateral sulcus, filling the rectum.

A sigmoidal procidentia presents the same characteristics as those of the rectum

The disease is manifested by a cluster of small erosions (eroded vesicles) on the glans penis or corona, sometimes associated with a group of typical herpetic vesicles on the shaft Herpetic infection of the genitalia of women, as of men, may be primary or recurrent The primary disease is manifested by the appearance of superficial erosions on the labia majora, labia minora and distal vaginal mucous membrane These ulcers are tender and covered by a grayish yellow membrane. The annoying discomfort usually subsides within a few days but may persist for a week or two There is a tendency for the disease to recur with similar erosions of clustered vesicles revealing an ulcerated region covered by the grayish yellow membrane.

Phimosis. Phimosis, classified as (1) congenital and (2) inflammatory, is ordinarily a symptomless defect in the preputial orifice characterized by muzzling or closure of the skin over the distal end of the penis so that the skin cannot be drawn back over the glans. Phimosis late in life may give rise to symptoms as follows: (1) retention of smegma, (2) preputial concretions, (3) adhesions, (4) balanoposthitis, (5) paraphimosis, (6) gangrenous belanoposthitis and (7) carcinoma.

Smegma accumulates behind the adhesions slowly in some persons, rapidly in others. The retention of smegma is a factor which predisposes to balanoposthitis and probably carcinoma Retention and ammoniacal decomposition of drops of urine, mingled with smegma, are the usual cause of the formation of preputial concretions and odors The tight foreskin, as the result of low-grade infection, forms adhesions to the corona and often over much of the glans and thus increases the difficulty in keeping the penis clean if such be desired by the patient.

Balanoposthitis. Balanoposthitis is an inflammation of the preputial cavity The membrane becomes reddened, mottled and moist The epithelium comes off in patches, leaving irregular excoriations which ulcerate and discharge pus There is a burning soreness with itching intensified by urination. Shallow ulcerations may occur In the severe forms of the disease there are fever and inguinal adenitis In a chronic balanitis of phimosis the mucous surface of the prepuce is granular and may become condylomatous.

In localized perimeatal balanitis of the tight meatus the inflammation may extend to involve the frenum. In time the meatus becomes so dense that the lesion cannot be differentiated from carcinoma except by biopsy.

Balanitis is obvious. The diseases to be distinguished are herpes progenitalis, lymphogranuloma inguinale, chancroid, chancre, tuberculosis and carcinoma.

Paraphimosis. This condition is characterized by a tight retracted prepuce which will not return over the swollen glans At times two folds appear, the fold nearer the root of the penis containing the constriction which ulcerates

Before the edema becomes fixed, the prepuce can be replaced in two stages, thus Evacuate the edema from the glans and foreskin to the subcutaneous tissue of the shaft of the penis by squeezing it from the glans toward the shaft Then seize the penis behind the paraphimosis in the fork between the index and middle fingers of the two hands With each thumb make pressure on the glans laterally, not from before backward, pressing the remaining edema slowly from the glans and gently urging the glans into the ring of tight foreskin It slips back suddenly If the prepuce cannot be reduced, the constricting ring must be cut

Gangrene of the penis and scrotum may occur as the result of a virulent infection of the skin and subcutaneous tissues of the debilitated and the aged man

Tuberculosis. Tuberculosis of the skin of the penis is said to occur by contact inoculation either orally or genitally. Either of these modes of infection must be rare Sexual relations continue between spouses during the early years of renal tuberculosis without resultant inoculation The disease may spread locally into the anterior urethra but no further unless stricture results

Lupus and the other forms of cutaneous tuberculosis may appear on the penis

Anal epithelioma, as the disease progresses, ulcerates, discharges foul, irritating, putrid material, bleeds on the slightest trauma, and causes severe pain and tenesmus on defecation. At its various stages anal carcinoma may resemble anal fissure, lymphogranuloma venereum, tuberculous and syphilitic lesions. A biopsy should be performed to prove the diagnosis.

The prognosis is bad, regardless of the treatment instituted. Often these lesions develop into large ulcerating, sloughing lesions which cause an indescribable degree of severe and constant pain The tumor ulcerates widely, into the pelvic viscera and often into the bladder. The malodorous blood discharge and the widely ulcerated perineal region are unavoidable despite any known treatment.

THE MALE GENITAL ORGANS

THE PENIS

Congenital Malformations. Either the absence or the doubling of the penis is very rare The penis may remain rudimentary If the lips of the slitlike urogenital opening on the undersurface of the penis fail to fuse anywhere along their extent, hypospadias results; this is a common occurrence in false hermaphroditism simulating the female type

Priapism. Priapism may be defined as persistent, painful, abnormal erection of the penis without sexual desire It exists in three forms. (1) the purely neurofunctional priapism, (2) that which results from disturbances in the local circulation and (3) that of unknown causes The first form is observed after injury of the nervous channels, as in fractures and dislocations of the vertebral column involving compression of the spinal cord, in tuberculosis or tumors of the spinal cord; in tabes dorsalis, and occasionally in other diseases of the central nervous system

Priapism of local origin is observed in cavernitis due to gonorrhea, to vesical stone, or to phagedenic ulcer of the prepuce; in the presence of neoplasm of the penis, which has invaded the corpora cavernosa, and after trauma with hematoma in the corpora cavernosa There is also priapism in leukemia, hemophilia, typhoid fever, tuberculosis, sepsis and acute articular rheumatism Priapism is often accompanied with severe pain It may become complicated by gangrene

Chordee. When the urethra is inflamed, the exudate may involve the corpus spongiosum surrounding it and prevent it from expanding In erection the organ assumes a downward curve, a condition designated as chordee It disappears with the subsidence of the inflammation

Diseases of the Skin and Subcutaneous Tissues of the Penis. The skin of the penis is thin, loose, free from hair except at the root, and has beneath it some fibers of the dartos muscle. The skin projects over the glans, forming the prepuce, and is attached to the neck or collum glandis and underneath as far forward as the urethra, forming the frenum The connective tissue beneath the skin is loose and free from fat A fibrous sheath (Buck's fascia) surrounds the corpora cavernosa and corpus spongiosum and binds them together

The lymphatics of the prepuce and skin drain into the inguinal nodes, those of the glans empty into the nodes just inside the abdomen Since the lymphatic radicles anastomose at the root of the penis, a lesion on one side of the organ may involve the lymphatic nodes in the opposite inguinal region

There are sebaceous glands in the skin of the penis near the skin of the scrotum which may become infected, red, and swollen and discharge a tiny drop of pus Cysts may occur in these glands A chancre on the skin over the shaft of the penis is rare. Viral lesions caused by the psittacosis-lymphogranuloma venereum group rarely occur on the penile skin

Herpes Progenitalis. Herpes progenitalis is a vesicular eruption occurring over the genitalia of men and women. It is caused by the herpes simplex group of viruses It occurs more commonly on the penile skin than on the genitalia of women. It often follows sexual intercourse.

cavernosa may occur. It affects only the laterodorsal terminal two thirds of the erectile bodies. The condition is of unknown origin.

The disease begins with a mild pain on erection or with a painless deviation of the erect penis The pain may be short-lived, and without treatment it will cease within a year. The deviation on erection, upward or to one side, increases for a time and then often tends to grow less. The patient ceases to be alarmed and accommodates himself to the permanent deflection Those who have extensive lesions may be unable to have erections. Flaccidity of the corpora, distal to the lesion, is frequent and often constitutes the chief complaint

The lesion may be so small as to be impalpable in the flaccid penis and is made apparent only by the deflection on erection. When the lesion is palpable, it is hard and flat and somewhat irregular and is within the corpus.

Fracture of the Penis and Extravasation of Urine. Fracture or rupture of the corpora cavernosa may occur from violence. The extravasated blood is absorbed and the laceration heals with a scar In erection this part does not expand, hence deformity and distortion with interference of function may result

Urine may invade the penis beneath the fibrous sheath but does not invade the glans because the sheath stops at the collum glandis (see Perineal Fascia and Muscles, p 393)

Benign Tumors of the Skin of the Penis. Papillomas of the skin of the penis, the so-called venereal warts, appear within the tight preputial cavity or, in the female, within the vulva They may attain an enormous size and become malignant. All urethral papillomas should be suspected of malignancy.

Condylomata lata, broad masses of papillomas about the moist creases of the penis, the scrotum and especially the anus, are usually due to syphilis.

Lipoma may occur in the perineum where it forms a bosselated ovoidal mass.

Malignant Tumors of the Penis. Cancer. Epithelioma or a squamous cell carcinoma of the penis is a slowly progressive tumor which often does not metastasize readily The average age at the time of the first symptom is 50 years. No authentic instance of the disease has been reported in a Hebrew circumcised at birth. Jewish women rarely have carcinoma of the cervix These two observations may indicate that here are two diseases not common to Jews At least, the value of circumcision as a preventive of carcinoma of the penis will have to stand on its own merits, it does not receive impetus by the citing of Jewish records. It is in non-Jewish persons that the disease appears most frequently. There is no doubt, however, that a long or a tight prepuce is present in most of those who have carcinoma of the penis

The common situation of cancer of the penis is about the corona of the glans The lesion may be papillary The tumor becomes infected early, ulcerates and sloughs Penile cancer usually metastasizes uniformly to the lymph nodes Occasionally a highly malignant lesion will metastasize to the bones and to the lungs.

The tumor often is hidden from the patient's view by the tight prepuce The complaints are referable to the infection In some instances the initial symptom is a lump under the prepuce or the presence of a bloody discharge from the phimosis

On examination, not infrequently it is necessary to make a dorsal slit in the prepuce in order to secure sufficient retraction for an adequate inspection of all the parts The appearance of the tumor and its palpable features is variable, from a small lump to a large, extensive, fungating, ulcerating lesion. The inguinal lymph nodes are often palpable. The enlargement of these nodes may be due to the malignant disease or to infection.

The venereal wart, condylomas, granuloma inguinale, and tuberculous lesions resemble cancer in some instances so closely that there is no safe criterion for the diagnosis except biopsy. Involvement of the lymph nodes can be proved by biopsy. If the corpora are definitely invaded with carcinoma, it must be assumed that the

or the scrotum Multiple tuberculous nodules have occurred in the corpora cavernosa and corpus spongiosum.

Cutaneous tuberculosis situated on the external genitalia of men has to be distinguished from soft chancre Soft chancre, in men, may occur on any part of the anorectal skin.

Soft Chancre. There are three infections of the external genitalia and anorectal regions of both men and women which are characterized by ulcerations and inguinal lymph-node involvement and abscess formation. (1) soft chancre, (2) granuloma inguinale and (3) lymphopathia venereum. The similarity of manifestations of these diseases and in the terminologies is confusing (see Diseases of the Female Genitalia, p 440).

A soft chancre results from an infection by the bacterium *Hemophilus ducreyi* (Ducrey's bacillus) Granuloma inguinale is caused by a bacterial infection; the specific bacterium is unknown but it characteristically forms Donovania granulomatis Lymphogranuloma venereum is caused by a filtrable virus

The soft chancre or chancroid is caused by *Hemophilus ducreyi* This organism appears in the purulent discharge from the soft chancre or chancroid of a venereal disease for which it is responsible. The morphologic structure of the organisms in local lesions is characteristic, chains of small gram-negative bacilli occur in strands. A saline suspension of killed *Hemophilus ducreyi* serves as a good antigen for diagnostic cutaneous tests

Soft chancre with associated abscess in inguinal lymph nodes is perhaps 15 times as common in men as in women It has been suggested that the causal agent, *Hemophilus ducreyi*, may be carried in the vagina without producing symptoms or ulcerations. It is transmitted by sexual intercourse However, infections may occur through contaminated towels and instruments, uncleanliness, and vaginal or urethral discharges In women chancroids occasionally occur round the vestibule, on the labia and occasionally on anal tags

The incubation period is up to 5 days, at the end of which a small reddish macule appears on the genitalia which soon becomes a pustule This ruptures to form a circumscribed ulcer with sharply defined, irregular, undermined edges and a gray, necrotic base The ulcers are multiple, as a rule, extend peripherally, and coalesce to form large, irregular ulcers with surrounding inflammatory areolae, which are circular or oval, rather soft and covered with an abundant, purulent secretion. These ulcers are extremely painful and tender The inguinal lymph nodes are swollen and tender and are termed *buboes*.

The diagnosis of uncomplicated chancroid is based on the identification of *Hemophilus ducreyi* on smear from a characteristic ulcerative lesion, a positive reaction to Ducrey vaccine, absence of *Treponema pallidum* on darkfield examination and negative Wassermann and Frei reactions. Failure to demonstrate Ducrey bacilli on smear does not necessarily rule out the disease. In lesions which are contaminated or treated with caustics, or of long duration, with sloughing areas, it is difficult to obtain the organism

Reaction to Intradermal Injection of Ducrey Vaccine. The reaction following the intradermal injection of 0 1 ml of Ducrey vaccine is specific At the end of 48 hours a papule 10 mm in diameter, surrounded by a zone of erythema 5 mm wide, denotes a positive reaction. A negative reaction leaves little to be seen at the site of inoculation The reaction becomes positive between 8 and 15 days after the appearance of the local lesion. A negative reaction after this time rules out a chancroidal infection in about 95 per cent of cases. A positive reaction may mean that the patient has a chancroidal lesion at the time the test is performed or that he has had a chancroidal lesion at one time. The reaction probably remains positive throughout the patient's life,

The disease may yield to treatment with sulfonamides

Fibrosis of the Sheath of the Corpora Cavernosa (Peyronie's Disease). In men between the ages of 30 and 60 years fibrosis of the sheath of th

A slight degree of stricturing causes no symptoms and requires no attention unless the patient has a chronic urethritis such as occurs in gonorrhea In some instances a gonorrheal infection may not be necessary for the origination of the urethritis A simple urethritis, with discharge so profuse as to be mistaken for gonorrhea, may be due to a strictured meatus, not necessarily tightly strictured, and disappears on correction of the stricture. Some aging men who have symptoms similar to those resulting from a large prostate gland are relieved by meatotomy.

Small strictures may interfere enough with the discharge of urine finally to injure the kidneys sufficiently to cause renal insufficiency, which may become manifest at any age, sometimes in youth, sometimes not until old age

Strictures of the posterior urethra of congenital origin are often caused by valve-like structures which have definite relationship to the superior or the inferior crista of the verumontanum. The symptoms appear in infancy, in childhood or in early adult life The stream is dribbling and the bladder distended when retention is great, but when the retention is slight, the bladder is not distended and the symptoms may be obscure. As the result of the retention of urine, soon there is an infection of the upper part of the urinary tract and perhaps finally renal insufficiency

The patient often has lost weight and is pale There may be dribbling of urine as if enuresis were present Patients who have had symptoms for a long time may be dwarfed and infantile, as is observed in so-called renal rickets.

There is no interference to the passage of a catheter, which usually reveals the presence of residual urine An intravenous urogram discloses the impairment of renal function and the dilatation of the upper urinary organs. If renal function is impaired, an hour or two must elapse before a satisfactory film can be obtained. The valve is identified through a urethroscope. It may sometimes be seen by cystoscope

Epispadias is rare The urethra lies ectopic as a groove for varying distances along the top of the corpora cavernosa. The penis is wide and short The urethra of the exstrophied bladder is epispadic and the epispadic urethra without exstrophy is usually incontinent

Hypospadias situated in the balanic or penile urethra is but an arrest of the closure of the urethra in these segments. There are varying degrees of lack of closure, however, and thus these malformations range all the way from pseudohermaphroditism to simple hypospadias.

The urethra opens at the frenum or just back of it in balanic hypospadias, and on the underside of the shaft of the penis in penile hypospadias. In penoscrotal or perineoscrotal hypospadias the urethra opens on the anterior or posterior face of the scrotum but always beyond the sphincters. The urethral opening is often deformed and is congenitally strictured

The penis beyond the urethral opening is deformed The glans is wide and split, as it were, by the failure of the floor of the urethra to unite. This broad glans is tilted downward as though pulled over by the shortened urethra Its undersurface is often marked by an indentation or a little pocket at the site of the lacuna magna The congenitally split prepuce, divided on the ventral surface, is piled up on the dorsum in irregular folds.

The tight meatus may cause urinary frequency or infection, but the essential

scrotal hypospadiac

Nonspecific Urethritis. Inflammations of the urethra may be (1) bacterial, (2) parasitic, (3) traumatic or (4) irritative. A distinctive difference between nongonorrheal urethritis and gonorrheal urethritis is that gonorrheal urethritis begins at the meatus, whereas all other urethral infections generally originate in the prostate.

deep pelvic chain of lymphatic structures is involved and that whatever treatment is considered is likely to be only palliative.

Amputation should be done in all cases, for if metastasis is not present, amputation will cure the condition and if it is present, the procedure will get rid of a badly infected, odorous, primary tumor

THE MALE URETHRA

(*Urethra Virilis*)

The male urethra varies greatly in length, and therefore only average measurements can be given In the adult its length is about 8 inches (20.3 cm); of this, 1¼ inches (3 2 cm.) is prostatic, ⅕ inch (0.5 cm.) being in the bladder wall; ⅖ inch (1 cm.) is mebranous, a little more than 6 inches (15 2 cm.) is penile Its caliber varies, being smaller at the meatus and in the membranous portion than elsewhere The meatus admits a No 24 French sound (often larger), the membranous portion a No. 26 to a No 28. The prostatic portion is the largest, admitting a No. 32 sound The bulbous portion is almost as large, admitting a No 30 to a No. 32. Therefore a sound which passes the meatus should find no further obstruction. The fossa navicularis just beyond the meatus is larger than the rest of the urethra.

If urine begins to flow when a catheter is introduced about 8 inches (20.3 cm), it is safe to assume that the urethra is of normal length. If the bladder is distended, as soon as the catheter passes the membranous portion, about 6¾ inches (17 2 cm) from the meatus, urine may flow. In hypertrophy of the prostate the prostatic urethra is much increased in length and it may require a catheter 10 to 12 inches (25.4 to 30 5 cm) long to draw urine If a sound is stopped by a stricture less than 6 inches (15 2 cm.) from the meatus, it is anterior to the triangular ligament. The stricture is termed an *anterior stricture* Strictures where the subpubic curve is lowest, that is, in the bulbomembranous region, are termed *posterior deep strictures*, which are the commonest form Strictures of the prostatic portion of the urethra are almost unknown.

The urethra contains small mucous glands (glands of Littre) opening on its surface, and small pockets or recesses, called the *lacunae of Morgagni* The glands of Cowper open into the bulbous urethra just in front of the triangular ligament The racemose glands of the prostate open into the sides of the floor of the prostatic urethra, and the ejaculatory ducts open near the middle line just in front of the urethral crest (verumontanum)

Urethral Muscles. There are two sets of muscles in connection with the urethra; one set might be said to aid in expelling the urine, and the other, in retaining it. The expulsors are the longitudinal and circular fibers surrounding the urethra just outside the mucous membrane and the accelerator urinae or *bulbocavernosus* muscle The sphincters are the *compressor urethrae* or *external sphincter* muscle, and the internal sphincter at the neck of the bladder

Malformations. Important malformations of the male urethra and its accessory glands are of rare occurrence and consequently not all of them will be discussed

Absence of urethra is associated with absence of penis and also may exist when the penis is present There is complete retention of urine, and the infant dies unless the bladder drains through urachus or bowel Death usually ensues within a week or 10 days *Atresia* occurs either at the meatus or at the prostatic urethra. The condition is usually fatal if some arrangement cannot be made to get rid of the urine

Congenital stricture at the meatus may be only a slight narrowing of the orifice due to a fold of mucosa that elevates the floor of the canal. Such a constriction is of no significance unless the patient contracts gonorrhea or until instrumentation becomes necessary. The stricture may be so small that only the finest probe will enter. The narrowing may be at the meatus or at the inner end of the fossa navicularis or both.

Good evidence does not exist of any degree of natural immunity to gonococcal infection. The girl child is the most susceptible If any degree of acquired immunity exists, it is not measurable. There is no infection immunity such as exists in tuberculosis and syphilis That is, fresh infections may be superimposed on more chronic ones. One attack of the disease does not protect from future reinfection.

The incubation period of gonorrhea varies from 2 to 7 days. The most accurate information concerning the incubation period of this disease has been obtained from experimental inoculations. Under these conditions the urethritis is evident within 2 to 5 days.

Acute Gonorrheal Urethritis. The initial symptoms of an acute gonorrheal infection are those of acute anterior urethritis. There are a teasing sensation, a mucopurulent discharge and slight inflammatory swelling of the lips of the meatus. In from 1 to 3 days the meatus becomes swollen, the discharge thick, profuse and purulent, and urination and erections are at least uncomfortable and perhaps painful.

The inflammation of the urethra with a *second attack of gonorrhea may be so* mild that it scarcely invades the submucosa. The discharge is mild, erections are not *painful If the infection is unusually intense, hematuria may occur as* well as urethrorrhagia from bleeding of the anterior urethra.

Examination reveals mucopurulent urethral discharge. The diagnosis is established by positive smear and culture for the gonococci.

The complications of acute urethritis are abscess of the anterior urethral glands, periurethral abscess, cowperitis, spongiitis and cavernitis, balanoposthitis and lymphangitis and lymphadenitis These complications can rarely be separately identified clinically since small abscesses occur as the result of obstruction of crypts and glands, as a part of the acute infection, and are important in the production of the symptoms of the disease. The most frequent form of periurethral abscess is the frenal abscess It scarcely ever abates without suppuration, often requiring incision After incision it may continue indefinitely to discharge a secretion containing gonococci.

The less frequently occurring complications may be enumerated: (1) Periurethritis along the pendulous urethra occurs as small, hard nodular points of tenderness Introduction of a sound may be necessary in order to palpate them. These points, too, harbor the gonococci (2) Abscess of Cowper's gland is not recognized until the abscess has burrowed along the perineal fascia and its reflection and presents itself at the penoscrotal angle, where it bursts or is incised The original focus can be diagnosed by finding that the cavity runs back to the membranous urethra and not to the prostate (3) Inflammation of the erectile tissues, other than the brief pains of chordee, is rare (4) A lymphadenitis originating from secondary infection from other pyogenic organisms is frequent and in rare instances causes suppuration

The diagnosis is made by stained smears which are microscopically studied for the presence of intracellular gram-negative cocci.

There is evidence of a gonococcal complement fixation antibody which is acquired slowly after the onset of the infection The complement fixation test in gonococcal disease has not attained general acceptance.

Acute Posterior Urethritis and Prostatitis. Posterior urethritis and prostatitis are always a part of an acute gonorrheal urethritis As the infection varies in degrees of severity, so do the manifestations of its *urethral distribution vary.*

The symptoms of posterior urethritis and prostatitis are frequent, urgent and painful urination with terminal hematuria There is pus in the "second" or residual urine. The pain of the second infection or the first mild infection is no more than an itching sensation referred to the end of the urethra. Posterior urethritis with a first severe attack of gonorrhea is likely to be intense As the muscles contract to expel the last drops of urine, the resultant pain is often a series of spasms that may

The types of *bacterial urethritis* are (1) gonorrheal, (2) urethritis due to an indwelling catheter which disappears when the catheter is withdrawn, though a mild prostatitis is likely to persist; (3) urethritis by extension of pyogenic or tuberculous infection originating in the prostate, and (4) metastatic urethritis occurring in a canal damaged by previous inflammation. Spontaneous severe urethritis may develop when uncontrolled diabetes exists.

Parasitic urethritis may occasionally be caused by trichomonas. Trichomonas infections are common in the male urethra. Feo found 144 infected men in a group of 926. Separating this group into white and Negro men, the percentage incidence was 12 and 16.5 respectively. Of the 926 men examined, 246 were classed as having nonspecific urethritis. However, in all of these the urethritis was not due to trichomonas. The percentage incidence of nonspecific urethritis which may be attributable to *Trichomonas vaginalis* was 36 9. The entire group of *Trichomonas vaginalis* positive men was relatively free from symptoms. A discharge may be noted which is characteristically small in amount, thin in consistency and of a dirty white color. Microscopically this discharge shows a few epithelial cells and a moderate number of pus cells and trichomonads. Some of the stained smears were similar to vaginal ones from cases of *Trichomonas vaginalis* vaginitis as to number of trichomonads and types of bacteria. The male is the important transmitter of *Trichomonas vaginalis* infection, while the female eventually becomes a reservoir of infection

Traumatic urethritis is due to rough passage of instruments, urethral stone, foreign body or cauterizing injections The more serious and complete stricturing of the urethra is often due to trauma as the result of external violence

Irritative urethritis is due to the excretion of irritating substances in the urine, for example, cantharides, turpentine, arsenic and potassium iodide Irritation from urethral instillations of caustic substances, such as silver nitrate solutions, may be severe and serious.

The symptom of nongonorrheal urethritis is a discharge of pus from the meatus. This symptom is mild and inconsequential as compared to the syndrome of acute gonorrhea In diagnosis the absence of gonococci must be proved by urethral culture on the proper media

Posterior Urethritis. The lesions of chronic posterior urethritis are (1) diffuse inflammations, (2) granulomas, (3) cysts, (4) deformities due to operation or to rupture and scarring of a prostatic abscess and (5) verumontanitis and utriculitis.

The symptoms of chronic posterior urethritis are often mild and manifested by a lack of erection, premature ejaculation, painful ejaculation, and pain in the perineum, in a testicle or in the sacrum. These symptoms are like those often attributed to verumontanitis, for instance, absence of ejaculation, painful ejaculation, discomfort of various types in the perineum, and various reflex pains.

The diagnosis is established by endoscopic examination.

Urethral Gonorrhea. Urethral gonorrhea is caused by the gonococcus, which belongs to the family Neisseriaceae, genus *Neisseria. Neisseria gonorrhoeae* is a gram-negative coccus which is the type species To the same family and genus belong also the meningococcus and several nonpathogenic inhabitants of mucous membrane

Neisseria gonorrhoeae is the causative agent of gonorrhea and of ophthalmia neonatorum. The organisms appear in the exudate of acute gonorrhea as diplococci, flattened or slightly concave and crowded together in pairs.

Gonorrheal infection occurs spontaneously only in man. The gonococcus causes infection of the genitalia and the genital tract generally, and may give rise to conjunctivitis, cystitis, proctitis, hepatitis and stomatitis The septicemic manifestations ... con- ... and

may progress to complete pathologic amputation of the penis. This too is rare and the diagnosis is not made

Stricture. As chronic urethritis heals, a scar is formed A stricture is the scar that results Strictures external to the bulbous urethra are termed *anterior* strictures. Those beyond this point are *posterior* or deep strictures. Strictures are classified as *inflammatory* and *traumatic.*

Inflammatory Strictures. Severe strictures result from gonorrhea or are complications thereof. Usually only mild strictures result from nongonorrheal inflammation

Strictures as the result of gonorrhea are more frequent after virulent infections than after mild infections For instance, the more intense the chordee, the more frequent and violent the relapses and the longer the gonococcus can be found in the discharge, the greater is the probability of strictures

Inflammatory stricture may result from scarring about the obstructed and chronically inflamed glands or lacunae. The overdilatation of a stricture may be followed by a more severe stricture Suppuration may follow overdilatation or may occur spontaneously. The direction that a suppurative process takes is determined by the fascia. If a prostatic abscess bursts backward, or suppuration following overdistention occurs in the same place and does not drain forward into the urethra, the pus either reaches the ischiorectal fossa and appears at the surface in front of or alongside of the anus, or is confined by the fascia

The following enumeration lists other suppurative processes which complicate stricture. (1) The suppuration of prostatic abscess, especially if due to tuberculosis, often reaches the surface in the perineum or may extend forward to the scrotum and up into the groin between the penis and the spermatic cord. Thence it spreads upward and outward toward the loin, beneath the deep layer of the superficial fascia (2) Suppuration in Cowper's gland extends forward and passes along the urethra to the penoscrotal angle and surface of the scrotum (3) Suppuration from the bulbous urethra usually breaks directly into the perineum, whence it extends to the ischiorectal fossa, scrotum, groin, pubes or anterior abdominal wall. (4) Suppuration from the penile urethra bursts directly through the skin of the penis. (5) Inflammation and dilatation of the bladder, the ureters and the kidneys are late results of strictures A stricture unaccompanied by sclerosis or spasm of the vesical neck does not cause partial retention of urine Stone in the bladder is rarely the result of stricture

Traumatic Strictures. The penile portion of the urethra may be cut, torn, or broken by external violence A crushing force applied to the perineum causes a stricture at the bulbomembranous junction by bringing the urethra sharply into contact with the undersurface of the pubis, crushing it beneath the sharp edge of this structure Falling astride a fence or a fence post may cause a traumatic stricture in the posterior portion of the urethra These injuries to the urethra may be overlooked by the patient if they do not give rise to immediate hemorrhage or urinary retention The prostatic urethra becomes strictured when torn by disruption of the pelvis Trauma originating from within, such as ulceration from stone, foreign body or retained catheter, or injury by the sharp point of an instrument, usually affects the bulbomembranous junction of the urethra Stricture at the neck of the bladder results from chronic prostatitis and transurethral resection of the prostate.

Within one year after a severe inflammatory process or trauma most patients will have strictures with manifest symptoms A few will show no symptoms until after 5 years In an occasional patient the onset may be deferred for 15 years or even longer Organic stricture may exist for years, producing no symptoms and entirely unsuspected by the patient

The initial symptom is usually the presence of pus and heavy thick shreds of pus in the urine. After stricture formation which immediately follows gonorrhea the urethral discharge does not cease.

last for a few minutes after urination or may continue in the tonic spasm of strangury during the short period between successive urinations In these patients urination is genuinely agonizing.

Toward the end of the acute period of gonorrhea (2 months) the patient, even if untreated with antibiotics or chemotherapy, has no symptom other than a drop of pus at the meatus when he awakes in the morning (the morning drop). This drop of pus may be so mucoid that it may stick the lips of the meatus together.

The diagnosis is established by positive smears and cultures

The complications of acute posterior gonococcal urethritis are prostatic abscess, vesiculitis, epididymitis, cystitis, and occasionally pyelonephritis and peritonitis.

The distinction between acute prostatitis in which miliary abscesses have not yet appeared and *prostatic abscess* cannot be made clinically. The gonococcic prostatic abscess and *vesiculitis* have no distinguishing features from any other etiologic types of these diseases When there is *epididymitis,* there is vesiculitis. The *cystitis* of gonorrhea is a trigonitis It is an extension of the mucosal inflammation of the posterior urethra A general cystitis may occur in gonorrhea if there is a retention of urine

A nongonococcal pyelonephritis may occur in the course of gonorrhea

Chronic Gonococcal Anterior Urethritis. When the disease lasts for more than 2 months, the gonococci diminish in number in the pockets in the urethral wall, to be replaced by other bacteria which keep up a mild inflammation. If stricturing and poor drainage prevail in a debilitated patient, anaerobic bacteria may cause periurethral gangrene

The most persistent form of chronic anterior gonococcal urethritis is caused by a frenal abscess. The urethra may become free from gonococci only to be reinfected from this source The course of a chronic gonococcal urethritis is often a series of exacerbations of the acute process Apparent improvement or cure is followed by exacerbation, seemingly caused by indiscretion, by reinfection of the surface of the urethra from an infected focus.

The diagnosis is established by positive smears and cultures

Chronic Gonococcal Posterior Urethritis. The clinician can rarely obtain a positive smear for gonococci from the prostate or the vesicles The bacteriologists, however, can often get positive cultures

The inflammation loses its characteristic irritability, and the urethritis tends to run a milder and more even course after the gonococci have disappeared Many of these patients have a posterior urethritis by secondary invaders Although some of these patients have not had gonorrhea, it is their lot to have an irritable prostate which has been treated for gonorrhea which they did not have.

Prognosis in Urethral Gonorrhea. The foregoing description of gonorrhea in the male is becoming out of date since the advent of chemotherapy and antibiotics (duracillin). The following prognosis applies to those who have not been thus treated.

The average man should recover from gonorrhea in 3 months if he has no complications such as stricture, prostatitis, epididymitis or vesiculitis If the infection is complicated by a frenal abscess, the course may be indefinite It is most unusual for the gonococcus to persist in the male Prior to use of antibiotics many patients recovered from gonorrhea without or despite treatment

Chronic gonorrhea in women may almost last indefinitely

Amicrobic Urethritis. In France there has been described an increased incidence of amicrobic urethritis in men that has proved resistant to penicillin and sulfonamide compounds. Harkness has insisted that this infection is caused by a *virus* This form of urethritis may be associated with prostatitis and epididymitis.

Syphilis. Chancre of the urethra as a rule is not recognized. Chancre has not been described in the deep urethra. Gumma occurs in the corpora ca[illegible]a and

tinence. Diverticula of the penile urethra may produce a swelling of the ventral portion of the penis when the patient voids.

Visualization of the urethra by cysto-urethrography is the best method of diagnosis. Radiopaque substances injected into the urethra clearly outline the diverticular sac.

Tumors. The neoplasms of the male urethra arise from the epithelium. Tumors arising from other elements, such as sarcomas, are rare.

Benign Tumors. Benign papillary tumors occur in any portion of the urethra but are commonest in the posterior portion. These tumors of the male urethra usually are small delicate neoplasms. Histologically they are composed of epithelial cells, mitotic figures are not present, and there is no evidence of invasion or other signs of malignancy. Initial hematuria is the most frequent evidence of urethral papilloma. Tumors situated in the posterior part of the urethra may cause sterility by occlusion of the ejaculatory ducts The diagnosis is established by endoscopic examination and biopsy.

Malignant Tumors. Carcinoma is the commonest primary malignant tumor of the male urethra This lesion occurs most often in men between 40 and 50 years of age.

Cancer may arise in any portion of the male urethra There has been no significant difference in its frequency in the anterior and the posterior portions of the urethra Histologically these tumors usually are epidermoid carcinoma or adenocarcinoma. Primary carcinoma of the urethra metastasizes late in the disease

Slow stream, frequency, dysuria and hematuria are symptoms of primary carcinoma of the urethra. Considerable infection seems to be a feature of these neoplasms, and abscess formation and fistulas are common.

Diagnosis is established by biopsy Early diagnosis of urethral carcinoma is difficult. Symptoms are so suggestive of stricture of the urethra that many patients with urethral cancer have been treated for stricture. Tumors of appreciable size can be felt along the urethra. Any progressive narrowing of the urinary stream associated with a palpable mass along the course of the urethra should suggest carcinoma.

THE SCROTUM

Anomalies. Anomalies of the scrotum include underdevelopment of the scrotal [illegible]

[illegible]
However, the scrotum is peculiarly resistant to infections.

[illegible]

in appearance. Gangrene appears and spreads rapidly and soon the skin sloughs away The process extends beneath Colles' fascia and may spread into the groins and onto the abdominal wall. The testicles are left exposed Even after extensive involvement the process ceases suddenly, as it commenced, granulation appears and the scrotal skin regenerates quickly.

Gangrene is differentiated from phlegmon by the absence of history of disease causing extravasation of urine Phlegmon does not slough extensively One of each 5 who have the disease dies

Elephantiasis. Elephantiasis of the scrotum is endemic in many southern regions The disease is due to infestation by a nematode worm, *Wuchereria bancrofti.*

The symptoms of filariasis are episodes of lymphangitis, lymphadenitis and swelling of the scrotum Repeated attacks of the disease may result in enormous scrotal enlargements Except for this deformity, the physical condition of the patient is unaffected.

Frequent micturition, often painful, is due to straining to overcome the urethral resistance, prostatitis and cystitis. If there is pyelonephritis, the frequent urination may be a true polyuria

If a stricture becomes congested, it closes, and acute retention of urine ensues. If this retention is unrelieved, the progression is like that of an acute prostatic retention from benign hypertrophy.

As the stricture contracts, the urethritis grows worse and, sooner or later, produces a morning discharge (gleet). The morning discharge gets better or worse according to the degree of acidity of the urine and the amount of sexual indulgence. As the stricture tightens, the stream of urine is small and irregular. Erection is sometimes imperfect and painful

The pain on urination in stricture is due to prostatitis, cystitis or retention. It is perceived deep in the urethra, in the perineum, at the point of stricture, or near the glans penis

When gross hematuria occurs, it is often the only symptom of stricture noticed by the patient. The bleeding comes from a shallow ulcer and may be profuse The blood usually continues to drip after the close of micturition (urethrorrhagia).

DIAGNOSIS The diagnosis of strictures is made only by those trained to use the bougie and the sound (1) In stricture of the pendulous or scrotal urethra the bulbous bougie either fails to pass the strictured point or passes with a jump and is caught again by the stricture on withdrawal. (2) Stricture at the bulb is diagnosed by use of a sound A sound distinguishes stricture from spasm by the fact that, when it has entered the stricture, it is grasped on withdrawal. Blood follows withdrawal of the sound (3) Spasmodic stricture is a symptom, not a disease. It is a subjective spasm, created by an unduly irritable muscle because of urethritis or prostatitis Urethral spasm is often a postoperative complication (4) Traumatic strictures contract rapidly and are usually incurable The more extensive a stricture, the more irregular its surface, and the denser the cicatricial tissue composing it, the more difficult will be its treatment and the more dubious its cure.

If death results from a stricture, it is from septicemia, obstruction of urine and renal failure, or periurethral gangrene When the patient is debilitated, sudden death may occur after the passage of a sound.

Urethral Stones. Vesical calculi may pass into the urethra and become impacted along its course. Prostatic calculi occasionally erode through the mucosa and obstruct the urethra Primary urethral calculi may form behind a stricture or within a diverticulum Urethral calculi cause varying degrees of obstruction, depending on their size

Patients who have urethral calculi often are unaware of the presence of the stones The diagnosis frequently is made by the passage of some instrument into the urethra Characteristic grating then may be felt This sensation may be obtained at times when tough old strictures of the urethra exist so that stone is suspected although not present. Stones within urethral diverticula are detected by roentgenologic examination

Diverticula. Diverticula of the male urethra are uncommon They are classified as congenital and acquired.

Congenital Diverticula. Diverticula of this type are said to occur most often on the floor of the penile portion of the urethra Their origin is thought to be due to incomplete fusion of that portion of the urethra which is derived from the phallic part of the genital tubercle with the portion of the urethra which is derived from the urogenital sinus.

Acquired Diverticula. The acquired types of urethral diverticula are due to the presence of stricture or stone, abscess formation or trauma The symptoms if present are those of chronic inflammation: dysuria, dribbling and incon-

The testis is covered by peritoneum, which is prolonged at its upper and lower ends The lower end reaches down to the internal ring and later contains fibrous and muscular tissue and passes through the inguinal canal to the lower part of the scrotum; it is called the gubernaculum testis It reaches its highest development in the sixth month, and its remains attach the testicle to the lower part of the scrotum as the ligament of the scrotum As the testicle descends, it is preceded in its descent through the inguinal canal by a fold of peritoneum, the vaginal process, which forms the tunica vaginalis over the testicle

The vaginal process may not entirely close, so that the peritoneal fluid passes down to the tunica vaginalis covering the testicle; this is called a *congenital hydrocele.* If the opening is large enough for intestine to enter, it forms a *congenital hernia.* If the opening is closed above, usually at the external ring, and fluid accumulates in the tunica vaginalis, it forms an *infantile hydrocele.* If a portion of the vaginal process persists somewhere along the spermatic cord between the internal ring and top of the testis, there is an *encysted hydrocele.* A hydrocele in the inguinal canal of the female is a hydrocele of the canal of Nuck.

Anomalies of the Testicles. *Anorchism* or *monorchism* is extremely rare unless there is in addition an absence of one or more of the other elements of the seminal tract The failure to find an undescended testicle on surgical exploration is not prima facie evidence of its congenital absence Likewise *synorchism* is not a good explanation for not finding the second testicle.

Polyorchism is rare, but when present, there is but one vas and the duplicated testicles are joined by the epididymis

The absence of one testicle is rare, but when one testicle is lacking, there is absence of the homolateral kidney also, for there is absence of the whole urogenital fold

In *cryptorchism* the ectopic testicle may be halted at any point of its normal descent. It may be situated anywhere throughout the length of the inguinal canal. In infancy retention in the canal is common Retention frequently occurs at the external inguinal ring, in the groin and in the proximal portion of the scrotum.

The ectopic testicle becomes sterile because of the slightly higher temperature of its bed in the groin or inguinal canal than of the normal situation in the thin-walled scrotum Puberty is the accepted dividing line in determination of normal development of the testicle. It is expected that placement of the testicle in the scrotum before puberty will result in normal testicular development in size and function Retention of the testicle above the external inguinal ring after puberty is accepted as proof that the testicle has failed to attain normal size and spermatogenic function

When both testicles are ectopic, there is no spermatogenic function, although the hormones that determine the development of the secondary sexual characteristics and preside over the growth of the prostate and seminal vesicles are produced in undiminished quantities The secondary characteristics of sex develop normally.

The undescended testicle is much more liable to malignant growth than the normally situated testicle In almost every instance, if the testicle does not descend, there is a congenital *hernial sac* above the ectopic testicle

Infections of the Testicles. Direct extension of inflammation from the epididymis accounts for most instances of local inflammatory disease of the testicles. Blood-borne infections of the testis occur in pyogenic generalized infections· mumps, syphilis, the rickettsial fevers and typhoid fever.

Epididymo-orchitis occurs as a complication of injuries and operations on the bladder and prostate. In severe epididymo-orchitis the substance of the testis is destroyed by acute inflammation and abscess formation The swollen scrotal contents cause considerable pain and discomfort The cord is enlarged and tender along its course, giving pain and tenderness in the lower part of the abdomen suggestive, at times, of acute appendicitis As the scrotal mass increases in size, it first is hard and then becomes fluctuant Acute, severe epididymo-orchitis is obvious

Lymphedema. Progressive lymphedema of the extremities and scrotum occurs among men who never have resided in the tropics. This condition is the result of obstruction of the lymph channels and like Milroy's disease of young women may be congenital in origin Rarely is there a history of any significant infection or injury

Tumors. New growths of the scrotum are not common.

Benign Tumors. The benign tumors may be enumerated: (1) Vascular neoplasms and an occasional accessory spleen in the scrotum are recorded as examples of tumors of congenital origin. (2) Sebaceous cysts are common. They appear as yellowish, round, freely movable tumors which vary in size and number The cysts are filled with thick, foul debris Usually scrotal cysts require no treatment. (3) Lipomas are composed of large lobules of well-encapsulated fatty tissue. Symptoms result only from weight and pressure (4) Connective tissue tumors of the scrotum are slowly growing, small hard neoplasms. (5) Myxomas of the scrotum occur as smooth, lobulated masses and may attain considerable size These neoplasms are said to transilluminate (6) Tumors of the lymphatic vessels occur as diffuse lesions The skin is edematous, indurated and often ulcerated These neoplasms are occasionally malignant (7) Hemangiomas originating in the subcutaneous tissues, may slowly enlarge. They are composed of masses of dilated blood vessels filled with blood.

Malignant Tumors. Most malignant tumors of the scrotum are epitheliomas

CARCINOMA OR EPITHELIOMA. Considerable interest is attached to carcinoma of the scrotum because of its rapid growth, high mortality and occupational incidence This was the first recognized occupational cancer.

Carcinoma of the scrotum may develop in workers in certain industries as a result of their occupation Chiefly these are chimney sweeps, employees in textile industries, and men exposed to tar, pitch and lubricating oils *Mule spinner's disease* is cancer of the scrotum occurring in men who work in the cotton industry where they are exposed to the carcinogenic agent present in mineral oil used for lubrication This disease has nothing to do with the faithful farm animal, the southern mule.

Carcinoma or epithelioma of the scrotum is epidermoid carcinoma The lesion starts as a small wart, which soon ulcerates The ulcer is hard and indurated and has everted edges. As the lesion advances, the lymph nodes of the groins become involved and are felt as hard, tender masses which also eventually ulcerate

Scrotal cancer metastasizes to the inguinal and femoral lymph nodes Crossed metastasis occurs frequently.

The diagnosis is established by biopsy Scrotal carcinomas are highly malignant tumors Even with early excision the prognosis is not good.

SARCOMA Sarcoma of the scrotum is rare

THE TESTICLES AND ASSOCIATED STRUCTURES

The Testicles. *The normal testicles are 1½ inches (3 8 cm) long, 1 inch (2 5 cm) wide, and ⅘ inch (2 cm) thick* If larger, they are either hypertrophied or diseased. They are firm to the touch If hypertrophied, their consistency is not materially altered, if diseased, they are usually harder than normal. If smaller, they are usually atrophied and besides the lessening of size are also softer and flabby in consistency

The testicles rest attached at the inner posterior portion of the scrotum and the long axis points upward, slightly forward and outward In the presence of hernia and hydrocele the testicle is to be felt for first at the inner posterior aspect of the swelling. If not found here, the testicle may be palpated anteriorly instead of posteriorly. The position of the testicle in the presence of hernia or hydrocele can also be determined by seeing its outline by means of a light placed on the opposite side of the scrotum.

Descent of the Testicles. The testicles begin to develop early in fetal life, at about the third month, below and in front of the kidneys, opposite the second lumbar vertebra.

pathic hydrocele is a slow accumulation of fluid within the tunica vaginalis for no known reason. The soft tumor of the testicle transilluminates, and on needle puncture yields clear, straw-colored fluid.

Hydrocele must be differentiated from hernia. Hernia does not transilluminate, gives an impulse on coughing and often can be reduced. Spermatoceles contain milky fluid containing spermatozoa and usually are situated at the upper pole of the epididymis. Chronic hydroceles with thickened sacs, if large and uncomfortable, may require excision

Neuralgia. True neuralgia of the testicle or cord is an ache, constant and mild, which often is of long duration. The ache or pain may be situated throughout the length of the cord or in the testicle. The pain may be centered in the epididymis. In instances of severe pain of neuralgic nature in the testicle, removal of the testicles will not relieve the pain. The operation will make the neuralgia worse.

Prolonged sexual desire may produce neuralgia (*stoneache*).

Tumors of the Testicles. Tumors of the testicles are both benign and malignant

BENIGN TUMORS Hyperplasia of the interstitial cells of the testicles may occur in children This condition may be accompanied by precocious bodily and sexual development. Gynecomastia sometimes is present Adenomas, fibromas and hemangiomas have been reported but they are rare. Simple cysts of the testis are rare So-called benign teratomas have been described, but these tumors sometimes are malignant since they have been known to metastasize.

Benign tumors of the testis can be differentiated from malignant neoplasms only by microscopic examination.

MALIGNANT TUMORS Malignant tumors of the testis are often a most dangerous form of malignant disease

Malignant testicular neoplasms have been reported from birth to old age, but they are commonest between 20 and 45 years of age with an average age of about 35 years The association of malignant tumors with cryptorchidism is well established

Friedman and Moore found, on examination of 922 testicular neoplasms, that 96 per cent of these new growths fell into one of the following categories. (1) seminoma (germinoma), (2) (a) embryonal carcinoma and (b) chorio-epithelioma, (3) teratoma and (4) teratocarcinoma

The *seminoma* is one of the commonest of malignant testicular tumors. Seminomas have less malignant characteristics than embryonal carcinomas in that they tend less to invade and destroy adjacent tissues They occur at a later age than other testicular neoplasms *Embryonal carcinomas* fortunately are less common than seminomas *Chorio-epitheliomas* of the testis are rare. These are small, soft, hemorrhagic tumors They grow very rapidly and have a poor prognosis Characteristic of chorio-epitheliomas are their rapid growth, early wide dissemination, lack of radiosensitivity and high titer of chorionic gonadotrophin in the urine Most of these tumors end fatally within a short time

Teratomas are bizarre neoplasms which contain differentiated adult structures such as bone, cartilage or well-formed organs resembling teeth and hair. Any organ of the body may be represented in these tumors. They are slowly growing neoplasms which constitute fewer than 1 of each 10 new growths of the testicles. *Teratocarcinoma* or embryonal adenocarcinoma usually consists of a mixture of teratoid elements in the rete testis, but the epithelial elements grow rapidly and soon overgrow the tissue of origin It is a highly malignant tumor

ENDOCRINE TUMORS OF THE TESTES. In this discussion it is convenient to consider that a testicular tumor may arise from any one of the four different cellular structures. (1) the supporting connective tissue, (2) the interstitial cells of Leydig, (3) the supporting cells of Sertoli and (4) the germ cells. Tumors arising from cellular structures other than the germ cells are scarce. Three in every 100 testicular

ORCHITIS IN MUMPS. Orchitis in mumps rarely occurs before puberty. After puberty it occurs in about 1 of every 5 who have the mumps Severe orchitis is followed by atrophy of the testis in about one half of the cases.

Orchitis in mumps appears within 3 or 4 days to 1 or 2 weeks after the onset of the parotid swelling The involved testicle or testicles are swollen, firm and very tender. Epididymitis of mumps may occur alone without orchitis or parotitis and in some instances with very little parotid enlargement.

Orchitis in mumps after puberty is a serious condition, for testicular atrophy and sterility may ensue if both testicles are affected.

SYPHILIS *Testicular involvement* is an early and a constant consequence of syphilis Two forms of *syphilis of the testicle are described, either a sclerotic or a* sclerogummatous lesion may be present.

Bilateral sclerotic orchitis is characteristic of late syphilis. The only symptom present is diminution or loss of testicular sensation.

Sclerogummatous syphilitic orchitis tends to localize in the rete and to extend thence to the epididymis and adjacent tunica vaginalis The gumma may be palpated as an irregular, insensitive mass on top of the testicle with a hard ridge along one side The opposite testicle is insensitive to pressure.

The forementioned findings of a testicular mass, with the opposite testicle in*sensitive, and the history of syphilis in the presence of positive serologic reactions,* are diagnostic

Torsion. The cause of torsion is often unknown to the patient If torsion is more than one half of a revolution and if it is not promptly untwisted, gangrene of the testicle and epididymis ensue.

Torsion may occur in infants, but in most instances, perhaps 3 out of 4, it occurs between the ages of 15 and 25 years; in the remainder it occurs in adult life. It is usually situated on the right side

Slight torsion may recur a number of times before the circulation is sufficiently injured to cause atrophy of the testicle The onset of the pain may be mild or severe. Often attacks of mild pain and swelling of the testicle occur and subside, to be followed by more attacks, thus simulating epididymitis of gonorrhea or recurring trauma

In severe torsion the gangrenous testicle within a few days reaches an enormous size and its sensibility diminishes, but pain and fever persist.

The diagnosis of complete torsion of the cord is established by the history and examination Mild torsion may not be recognized before it becomes complete *If mild torsion is diagnosed, the scrotum should be incised and the testicle* sutured to the scrotum Had the gubernaculum of the testes anchored the testicle tightly to the bottom of the scrotum torsion would not have occurred

Injuries of the Testicles. The testicles are protected against injury by their mobility and position Injuries occur from *direct blows and lacerations.* Causes of injury may be enumerated as follows. (1) Exposure to roentgen rays may seriously affect the spermatogenic elements of the testis. (2) Contusions of the testis result from direct blows. These injuries cause severe pain because of edema and regions of hemorrhage within the organ. Contusions of the organ may result in hydrocele, *hematocele and sterility* Piercing wounds of the testicle are often serious and are followed by hemorrhage (3) Lacerations of the testis may occur from penetrating wounds of the scrotum Lacerations require suture of the tunica albuginea to prevent herniation of the testicular tubules.

Severe injuries of the testicle are accompanied by shock Pain is severe The scrotum becomes enlarged and discolored.

l within the tunica vaginalis occurs as an *acute*
ele results from trauma, inflammation such as
es from testicular neoplasms. Chronic or idio-

has been the subject of considerable comment. Confusion regarding the value of these tests arises when it is not recognized that the hormone present in the urine in those who have testicular tumors is different from the hormone present in castrates and in women past the menopause. The presence of chorionic gonadotropic hormone in the urine of a patient who has a possible malignant tumor of the testicle is an evidence of the presence of a tumor containing chorionic tissue A decrease in the chorionic gonadotropic hormone means removal or regression of chorionic tumor tissue An increase means a spread of the disease or an increase of follicle-stimulating hormone with a synergistic effect on the chorionic gonadotropic hormone.

Since the reactions to the Aschheim-Zondek and Friedman tests often are negative in seminoma and other tumors of high malignancy, the value of these tests in diagnosis is limited. However, the presence of chorionic gonadotropic hormone in the urine means that there is an active tumor somewhere and suggests a bad prognosis. The amount of gonadotrophin present in the urine is significant. Patients whose urine contains 2,500 or more mouse units per liter are short-lived All of those who have 10,000 mouse units in the urine have been proved to have chorio-epithelioma.

Most teratomas (adult teratomas) without malignant elements are cured by orchiectomy alone Seminomas respond well to orchiectomy and external radiation and many of these tumors probably are cured. Embryonal carcinomas and terato-carcinomas have a higher mortality rate, and in these neoplasms radical surgical intervention may produce better results Chorio-epithelioma, generally, gives a poor prognosis although an occasional patient with this neoplasm has survived for a number of years

The ten-year survival rate for treated patients who had seminoma, as reported by Cabot and Berkson, was nearly 50 per cent as compared with a ten-year survival rate of about 25 per cent for patients with other forms of carcinoma

Tumors of the Testicular Tunics and Spermatic Cord. The majority of the tumors of the testicular tunics are of mesoblastic origin and are lipomas, myxomas, fibromas, or mixtures of cell elements. Sarcomas occasionally occur. All of these are rare tumors

Most tumors of the *tunica vaginalis* are benign A few epithelial tumors have been reported, all benign adenomas. Other benign neoplasms are lipomas, fibromas and myomas All the malignant tumors have been sarcomas The *tunica albuginea* gives rise to fibromas or sarcomas.

Tumors arising from the testicular tunics usually resemble testicular neoplasms and are treated as such A few benign growths have been removed by local excision

Tumors originating from the *spermatic cord* are all mesoblastic and usually benign The commonest tumor of the cord is the lipoma

The Spermatic Cord. The left spermatic cord is longer than the right, hence the left testicle hangs lower The cord is composed of the vas deferens with its artery and veins, the spermatic artery with its veins, the cremasteric artery, and the layers derived from the abdominal wall which extend to become the tunics of the testicle The vas deferens is a small, round, hard cord lying posteriorly which is palpable through the scrotum.

Varicocele. Varicocele is varicosity of the veins of the pampiniform plexus of the spermatic cord *Spontaneous varicocele*, a mild form of varicocele, is a common affection It occurs usually on the left side. The deformity makes itself manifest before the age of 25 years A *symptomatic varicocele* may occur as the result of pressure on the spermatic vein on either side or on both sides

Some patients with varicocele have hypochondriac complaints. Old men do not complain of varicocele Perhaps there is a slight dragging sensation in the groin On examination the vessels are dilated and feel like a soft tangled cord or a bundle of worms

tumors studied by Friedman and Moore were germ cell tumors. Of the germinal cell tumors, *those arising from the Leydig and Sertoli cells are rare,* but their clinical manifestations are complex, for the Leydig extratubular cells produce androgen and the Sertoli intratubular cells produce estrogen. Therefore a condition is originated in which a masculinizing and a feminizing hormone are being produced side by side in the same gland. If the Leydig cell secretion, androgen, is excessive during youth, a giant is the consequence. If the Sertoli cell secretion is increased, the youth is feminine in character

The chorionic cell tumors produce a luteinizing type of gonadotrophin If gonadotrophins are produced in excess, estrogen also is produced in excess and *gynecomastia ensues. It is said that* any male who has enlarged breasts suffers from an endocrine imbalance This may be true, but often gynecomastia is present in youth without evidence of endocrine imbalance (see Diseases of the Breast, Chapter 8). Gynecomastia may be associated with disturbed testicular function observed after trauma, cryptorchidism, senility, severe hepatic damage and the administration of stilbestrol.

The excess estrogen in those who have chorio-epithelioma of the testes is formed in the tumor itself and can be extracted from it. The extract (gonadotrophin) from chorio-epithelioma of the testis gives a biologic test similar to that of the pregnancy-urine test *It is the amount of gonadotrophin present in the urine which is* significant. Large amounts (10,000 to 100,000 or more units) may be present in the urine from one who has a chorio-epithelioma. The amount of gonadotrophins present is indicative of the mass of functional tumor cells present.

Malignant tumors of the testis metastasize by lymphatic structures along the spermatic cord to para-aortic lymph nodes, then through the prevertebral chain of lymph nodes through the mediastinum and along the thoracic duct to the left supraclavicular fossa and perhaps to the lung. Metastasis to the left supraclavicular lymph node is present in an occasional case. Crossed metastasis, at a high level, may occur. *Inguinal lymph-node involvement occurs when the tumor has involved* the scrotal tissue The size of the primary tumor has little to do with the onset of metastasis

Despite the ready accessibility of the organ, symptoms of tumor of the testis frequently are not noticed for a long time Large masses may cause dull, dragging discomfort The presence of an abdominal mass or backache, from involvement of retroperitoneal lymph nodes, may be the first symptom of testicular tumor. Some tumors have an onset resembling acute epididymitis. In many instances trauma brings the tumor to the patient's attention Often the first manifestation of these new *growths is a metastatic lesion found on routine physical examination,* or the presence of a metastatic nodule in a lung revealed by roentgenographic examination, or an enlarged left supraclavicular lymph node Hydrocele may be found in association with testicular neoplasm Gynecomastia may be present

The diagnosis is made by biopsy after removal of the testicle for a tumor. Biopsy of the suspected testicle is never performed, since this procedure is likely to spread tumor cells and lead to local recurrence. If it is strongly suspected that a malignant testicular neoplasm is present, the entire organ, with its tunics intact, is removed. Difficulties in the diagnosis of these tumors are many Testicular neoplasms have been mistaken *for hydrocele, hematocele, epididymitis,* orchitis and tuberculosis It

the mass feels heavy. If hydrocele is present, the fluid may be aspirated to provide better examination of the testicle The cord usually feels normal

The value of hormonal tests in the diagnosis of malignant testicular neoplasms

is made Orchiectomy should not be performed until treatment with antibiotics has been given a trial.

Tumors of the Epididymis. Primary tumors of the epididymis are rare. They are benign or malignant.

BENIGN TUMORS. *Spermatoceles* are common. They may reach several centimeters in size They contain a milky colored fluid and transilluminate. Almost half of the primary neoplasms of the epididymis, lipomas, adenomas, leiomyomas and angiomas, are said to be benign. Mesotheliomas are nonmalignant neoplasms primary in the epididymis

Benign tumors of the epididymis are small and cause no symptoms. The presence of these benign tumors is detected in the course of a physical examination. Only by histologic examination is the diagnosis established

MALIGNANT TUMORS These tumors are about equally divided in their origin from epithelium and mesothelium Pain and a solid mass are the manifestations of a primary malignant tumor of the epididymis The diagnosis is established by biopsy.

The Vas Deferens The vas deferens descends to the lower end of the testicle and, becoming much convoluted, forms the globus minor or tail; thence it ascends, forming the body, and finally at the top, receiving the efferent ducts, forms the globus major or head Between the body of the epididymis and testis is a pocket or depression called the digital fossa Attached to the upper end of the testis is a small flat body which is in front of the globus major Attached to the globus major itself is a small cystic pedunculated growth. Both of these masses are known as the hydatids of Morgagni, the former is the remains of the duct of Muller, the latter is derived from the wolffian body The vas deferens then ascends along the spermatic cord to the internal abdominal ring of the inguinal canal

When the vas deferens leaves the internal abdominal ring, it winds around the outer side of the deep epigastric artery and dips down over the brim of the pelvis 1½ to 2 inches (3 8 to 5 1 cm) posterior to the pubic spine It then runs downward and backward on the side of the pelvis In its pelvic course the vas deferens is not often the subject of clinical significance except in cases of undescended testis.

Deferentitis. Deferentitis is recognized clinically in both acute and chronic forms which often follow gonorrheal infections. Also both acute and chronic forms of tuberculous infections are observed

The *acute infection* may be recognized as a thickening of the seminal vesicle which is palpable at the external ring. Commonly deferentitis extends from a tuberculous epididymis backward up the vas deferens. Muscular trauma at the inguinal canal occasionally excites suppuration.

Chronic tuberculous deferentitis is an irregularly distributed lesion, palpably knobby, and usually most marked in the scrotal portion As in epididymitis, it is tender or insensitive in proportion to the acuteness of the infection

The Seminal Vesicles. The seminal vesicles are about 2 inches (5 1 cm) long and lie on the bladder above the prostate. When normal, they are not readily recognized by touch, but in disease they are easily felt

Anomalies. Anomalies of the vesicles are usually part of some general genital malformation When one of the vesicles is absent, the corresponding testicle may yet be present Extreme dilatation of the vesicles is probably always acquired

The ejaculatory ducts may empty into the ureters instead of on the edge of the prostatic utricle In a few cases they have been found to continue forward alongside of the urethra the whole length of that canal to the meatus.

Wounds. Operative wounds of the ejaculatory ducts are frequent. The patency of the ducts is imperiled by prostatectomy.

Cysts. A gradual dilatation results from inflammation of the vesicles until they become two or three times their normal size and even overlap in the median line Such dilatations have no clinical significance. In rare instances one seminal vesicle may become obstructed at its outlet and then it will enlarge and form a tumor about

Tumors. Tumors of the cord are rare A lipoma is about the only tumor of the cord. It is secondary to hernial lipoma, is usually small, and is present in an inguinal hernia.

The Epididymis. The epididymis may be absent or imperfectly formed Such abnormalities result in sterility if bilateral. Abnormal relationships between testis and epididymis occur in defects of the urogenital union as previously described

Epididymitis. Epididymitis occurs most frequently in young men who have urethritis and aged men who have infection which has followed instrumentation during the course of prostatism.

Epididymitis is classified as follows· (1) gonorrheal epididymitis, (2) metastatic or septicemic epididymitis, of which tuberculous epididymitis is an example, (3) epididymitis following instrumentation and (4) epididymitis from trauma, physical and perhaps sexual excesses.

Gonorrheal epididymitis is acute or, if mild at the onset, tends to become acute later. The least trauma excites to an acute relapse. This relapsing tendency is short-lived The relapses of epididymitis after intervals of months or years are not due to the gonococcus Suppuration in gonococcal epididymitis is common

Metastatic epididymitis arises from distant infections, as for instance infection of the upper air passages, particularly tuberculosis or an acute pyelonephritis or some other source. Epididymitis is usually due to *Escherichia coli* or to *Staphylococcus aureus*. The bacillary infection shows the same tendency to gross suppuration, to involvement of the testis and cord and to relapse, as the epididymitis of urinary disease. Staphylococcal infections show a tendency toward healing and less tendency to suppuration and to relapse unless originating from a septicemia

Testicular injury and an ensuing epididymitis may follow trauma to the testicle such as may be sustained from falling astride a fence or from injury incurred during horseback riding The symptoms and course depend on the severity of the trauma. Rarely is the testicle injured sufficiently to require its surgical removal.

Epididymitis from *sexual strain*, the colored man's "strain," is usually of gonorrheal origin.

SYMPTOMS Often the inflammation begins slowly but later flares into an acute attack. In still others it remains mild and localized to the distal portion of the epididymis.

The acutely inflamed epididymis swells within a few hours to several times its normal size The organ is exquisitely painful and tender, the pain extending to the sacrum and to the loin. The temperature rises to 103 to 104 F (39.4 to 40 C). Intense symptoms may continue for days until relieved by infiltration of the sheath, after which the suppuration burrows through the scrotal fasciae, reaches the skin, bursts and leaves a chronic fistula

EXAMINATION. The acutely inflamed epididymis is a swollen, edematous ridge surrounding the normal testis The epididymis may become a large tender mass There may be epididymitis, periepididymitis and deferentitis The deferential lesions may extend the whole length of the vas and may be most marked at the lower end of the vas or at the external inguinal ring.

DIAGNOSIS The physical findings and history are usually diagnostically definite Epididymitis is distinguishable from torsion by the fact that elevation eases the pain of epididymitis and accentuates that of torsion When a swollen epididymis is associated with prostatitis, the condition is usually epididymitis Tuberculous epididymitis can ordinarily be distinguished by the history and the associated lesions and by its slow chronic course and perhaps by suppuration However, the diagnosis often is not made until histologic study has been done. After any form of epididymitis the prospect of sterility (on the affected side) is great.

Sporotrichosis of the Epididymis. Sporotrichosis of the testis and epididymis may occur in the course of a cutaneous sporotrichosis, in which event the diagnosis

trarectal (seminal vesicular carcinoma) and rectal carcinoma is the mobility of the rectal mucosa over the mass

Diagnosis of primary carcinoma of the seminal vesicle can be established by biopsy and histologic study

THE PROSTATE GLAND

The normal prostate gland is 1¼ to 1½ inches (3.2 to 3.8 cm) wide, 1 to 1¼ inches (2.5 to 3.2 cm.) long, and 1¼ inches (3.2 cm) thick. A central depression on its rectal surface separates it into lateral lobes. The prostatic tissue is continued uninterruptedly across the median line in the form of a commissure Enlargement of this part

rare and probably not

Nocturnal Emissions. Nocturnal emissions, usually associated with dreams, occur in boys and in men Such an emission is simply the discharge of semen while asleep

The fears that boys and young men can build on this physical phenomenon may be excessive. The experienced adviser will not even suggest posterior urethroscopy to the patient who complains of only infrequent emissions until a thorough understanding is had of the psychologic aspects of the patient and an attempt has been made to establish an alleviation of fear and anxiety by exercise, cold baths and diversion in a normal and unmorbid society, to diminish the number of the emissions and to minimize their importance in the mind of the sufferer. If these measures fail, it may be necessary to have recourse to more formal psychic investigation and then to examine the posterior urethra

Nocturnal emissions may continue in aged men long after they have become impotent. Often it must be explained to these aging individuals that the occurrence of these emissions is a normal phenomenon and not the sign of latent virility.

Hemospermia (Bloody Ejaculatory Fluid). Hemospermia may be symptomatic or idiopathic in origin

Symptomatic hemospermia may arise from prostatitis or vesiculitis, prostatic concretions, tuberculosis, or carcinoma, or may be due to sexual excesses. Hemospermia and hematuria may occur simultaneously Symptomatic hemospermia is of no great interest, for this symptom alone cannot be evaluated and is thus termed idiopathic hemospermia

Idiopathic hemospermia is not accompanied by hematuria or by pain It is not associated with pus or with sexual strain Massage of the seminal vesicles will often but not always deliver a bloody fluid. The amount of blood in the semen varies The semen may appear as pure blood There may or may not be infiltrations palpable about the seminal vesicles The condition seems to occur in middle-aged men otherwise in good health The hemospermia may continue for many months or years and shows a great tendency to recur Its sole importance is often related to the apprehension produced by its presence

Prostatorrhea. Prostatorrhea occurs when the muscles of the prostate are relaxed so that movement of the bowels squeezes some drops of opalescent sticky fluid out of the meatus This is harmless

Acute Prostatitis. Acute prostatitis is probably always associated with varying degrees of vesiculitis and urethritis In young and middle-aged men acute prostatitis is often due to gonorrhea, acute infections of the upper part of the respiratory tract, pyelonephritis and urethral stricture and prostatic massage. In old men the causes are pyelonephritis, prostatism, acute respiratory infections and unnecessary prostatic massage.

Urination is frequent, painful and urgent A few drops of urine may pass involuntarily every few minutes

4 to 6 inches (10 to 15 cm.) in diameter The true nature of this midline pelvic tumor is not known until revealed by surgical removal and histologic study.

Concretions and Calculi. A number of concretions or small calculi may be present in the vesicles of the aged

Spermatic colic is rare even in those who have calculi. It may occur at the moment of ejaculation or during sleep. The pain is very sharp and colicky and centralized about an inch up the rectum, or at the neck of the bladder or to the testicle. A painful and deficient emission may ensue. The colic lasts from 10 to 20 minutes and then subsides A hot rectal douche or the introduction of a finger into the rectum with pressure on the offending organ gives relief

Vesiculitis. McCarthy and his associates ventured the opinion that vesiculitis is but a corollary to prostatitis. However, there are three main types of infections of the seminal vesicles. tuberculous, gonorrheal and nonspecific. Congenital anomalies, such as persistence of the müllerian duct or dilatation or stenosis of the ejaculatory ducts, seem to predispose to seminal vesiculitis. Congestion or distention over a long period as the result either of prolonged abstinence or of excessive sexual contact also predisposes to development of vesiculitis in the presence of adjacent or focal infection

The commonest form of seminal vesiculitis is produced by extension of infection *after posterior urethritis This regional extension, which sometimes follows instru*mentation of an infected urethra, occurs either by migration along the contiguous surface of the mucosa or by lymphatic invasion. Infection by means of the blood stream in the course of systemic disease or from foci of infection is possible, as is *secondary involvement from a focus in the epididymis.*

Prostatic disease which interferes with proper drainage of the ejaculatory ducts may set up conditions ideal for the development of vesiculitis Urethral strictures which interfere with the proper drainage of urine from the bladder may result in an infection of the urethra, bladder, prostate and seminal vesicles.

SYMPTOMS Dysuria, frequency and nocturia may be present and may be the only symptoms A morning urethral drop and a light thin watery discharge at the meatus during the day are often caused by a coexistent inflammation of the prostate and posterior urethra Frequent seminal emissions and early ejaculations are common Blood ejaculations are pathognomonic of vesicular involvement. Recurrent epididymitis usually indicates chronic infection of the vesicles

A dull pain or ache in the perineum is evidence of congestion due to prostatovesiculitis. This is characteristic of true visceral pain, which is diffuse, poorly localized and frequently of a dull, boring nature In the more acute processes the severity increases

Pain in the flanks, epigastrium, upper abdominal quadrants, lower abdominal quadrants and suprapubic region may occur as a result of infection in the seminal vesicles, prostate and adjacent structures There may also be present aches and pains of the groins, buttocks, perineum and lower extremities

On digital examination by way of the rectum the swollen and tender vesicle may be felt above and laterally to the prostate

The diagnosis of seminal vesiculitis is made from history, physical examination, microscopic examination of expressed secretions, endoscopy and vesiculography.

Carcinoma. Carcinoma of the seminal vesicles may resemble on palpation metastatic carcinoma situated on the rectal shelf.

The common tumors of the rectal shelf are metastatic lesions, and the greatest incidence of occurrence is found in carcinoma of the stomach It is frequent that patients who have *tumors of the rectal shelf* present a history of gastric complaints, while persons with primary carcinoma of the seminal vesicles frequently present a history of urinary difficulty and hematuria. A point of differentiation between ex-

Abscess of the Prostate. A prostatic abscess results from localization and resolution of prostatic tissue as a consequence of: (1) severe, acute or chronic infections of the prostate, (2) blood-borne infections during the course of severe respiratory infections, furunculosis, carbuncles and osteomyelitis and (3) instrumentation

There is a sudden onset of acute urinary symptoms such as frequent and difficult micturition Perineal pain is commonly present. Fever may reach 103 F or more Leukocytosis of 25,000 cells per cubic millimeter is commonly observed.

On rectal examination the prostate is swollen, tender and contains a fluctuant mass

Tuberculosis of the Prostate. Prostatic tuberculosis is symptomless except for the rigidity which involvement of the gland and of the overlying urethra imparts to the neck of the bladder The resultant achalasia is slight and the symptoms of the tuberculous cystitis are those present in a tuberculous prostate.

On examination there may be large and hard masses of periprostatic exudate These masses may also occur about the subacutely inflamed nontuberculous prostate gland.

The presence of tubercle bacilli in the vesical urine, and the absence of pus and bacilli in the renal urine, as obtained by ureteral catheter, associated with the physical findings of prostatitis or epididymitis, are likely to be symptomatic of tuberculosis. Final diagnosis awaits biopsy if this procedure is deemed prudent.

Tuberculosis of the Epididymis, the Vas and the Testicle. Tuberculosis of the external genitalia of the male may begin by focal infection from the blood stream, or by extension of the disease from the internal genitalia, or by extension to the tunica vaginalis from the hernial sac involved in a tuberculous peritonitis. Suppuration may occur at or below the external inguinal ring but scarcely ever above

The acute onset is characterized by swelling, fever, leukocytosis and pain; the chronic onset, initially by a lump which may be only slightly sensitive. The lesion may remain for years as a nodule of irregular shape without any tendency to suppuration. Such nodules are often felt throughout the epididymis.

the epididymis are important the little round nodules, the diffuse infiltration of the epididymis, the acute epididymo-orchitis; the frequency of hydrocele and abscess; and especially the frequent sensitiveness to pressure and the involvement of the vas.

The discovery of the tubercle bacillus in the urine, in the pus massaged from the prostate, or in the contents of hydrocele fluid or abscess, makes the diagnosis fairly certain

In infancy and childhood the accepted treatment is castration In adult life the tendency toward conservatism is good practice

Prostatic Stones (Concretions). Prostatic concretions occur in men more than 40 years of age. These concretions are small, round, black or brownish bodies impregnated with lime

No symptoms are att

nosed by the shadows

palpated to be thus diagnosed

Prostatism (Stenosis of the Bladder Neck; Hypertrophy of the Prostate). The syndrome of prostatism is produced either by narrowing of the neck of the bladder or by the presence of hypertrophy of the prostate in the neighborhood of the urethra Stenosis of the vesical neck and an enlarged prostate may coexist. However, sclerosis of the vesical neck differs essentially from hypertrophy of the prostate in that it may occur at any age.

The pain is situated on the undersurface of the urethra just behind the glans penis in the perineal region, down the thighs, in the rectum, over the sacrum and often above the pubes.

An acutely inflamed prostate gland may impede the outflow of urine. A fever, the temperature being 101 to 102 F (38.3 to 38 8 C), and leukocytosis are usually present.

The prostate is swollen, tense and tender The examination is performed gently in order to avoid injury and spread of the infection to the periprostatic tissue. If the periprostatic tissue is already inflamed, the outline of the gland is completely lost. The seminal vesicles may be palpable.

The diagnosis is evident from the symptoms and the examination. There may be pre-existing pyelonephritis or such may develop The inflammation in the vesicles often extends to one or both epididymides

Chronic Prostatitis. Chronic prostatitis may follow acute prostatitis, or its onset may be insidious

PATHOLOGY Periacinous infiltration and dilatation of the acini are the essential lesion of chronic prostatitis There usually are regions of normal tissue, and in some instances the diseased tissue is confined to that part of the gland adjacent to the urethra

The normal prostatic fluid is albuminous in appearance and has a characteristic odor It is alkaline to litmus and acid to phenolphthalein It contains gelatinous, transparent lumps of vesicular secretions, translucent lecithin bodies, columnar and round epithelial cells, fewer than 5 leukocytes to the high power microscopic field, a few corpora amylacea, and often spermatozoa Erythrocytes are present in the secretion obtained by massage of the prostate

Purulent prostatic secretion is thin, often yellowish and nonalbuminous in appearance The intensity of the infection is measured by the number of leukocytes and often by the number of bacteria present

SYMPTOMS Generally a chronic prostatitis is symptomless. When symptoms do occur, there is pain, usually in the perineum or occasionally in the lower part of the back The patient may describe it as a discomfort along the urethra, a burning, or a desire to urinate Frequent and difficult urination is due to the chronic posterior urethritis or to sclerosis of the vesical neck.

A disturbance of the sexual function if present is more likely due to age than to the disease Arthritis and other metastatic infections are rarely, if ever, due to inflammation of the prostate

EXAMINATION. The chronically inflamed prostate gland may appear normal on palpation Usually, however, the gland is enlarged The enlargement consists of a general softness of the lateral lobes At times the palpating finger may feel nodules of a somewhat increased resistance in the lateral lobes of the gland. Synchronously with the examination of a swollen prostate, there may be an outpouring of prostatic secretions from the meatus

Prostatic sclerosis is the result of chronic prostatitis of long duration. Scar tissue replaces the parenchymatous exudate, while infection continues in the acini The scar renders the prostate rigid to palpation and invades the neck of the bladder.

Vesiculitis is often a part of the infection which constitutes chronic prostatitis. This may or may not result in palpable enlargement. In longstanding instances the vesicle may be changed to an irregular cavity containing pus

DIAGNOSIS. The diagnosis of chronic prostatitis is made by the discovery of pus and often bacteria in the prostatic secretion Rectal palpation of the chronically inflamed prostate gland may reveal no abnormalities. In some patients the prostate may be tense, firm and bulging, or soft and boggy.

The prostate gland, once severely inflamed, may not become wholly normal. The boggy lobes sometimes but not always can be massaged free of pus, but they remain soft.

or to the symptoms. The symptoms of prostatism are associated with the retention of urine, urinary infection and hemorrhage.

Theories of the etiology of prostatic hypertrophy are enumerated thus: (1) benign ... a product of the disturbed sexual physiology of senility which is ...rnal secretion, (2) arteriosclerosis, (3) adenomatous ... of the breast, (4) myomatous and comparable to ... postgonorrheal, resulting from stricture of the prostatic ducts

PATHOLOGY. There is distention of the glandular acini with proliferation of the epithelium, resulting in the formation of masses of glandular tissue. The glands are surrounded by varying degrees of hypertrophied muscle and hyperplastic fibrous tissue

SYMPTOMS. An important symptom is nocturnal frequency of urination Before there is infection or retention of urine in the bladder, the patient has to arise several times at night to urinate. This nocturia begins by the patient being awakened with ... morn- ... the ... its coming in a small stream, and dribbling at the end of urination. When there is residual urine in the bladder or when the amount of residual urine increases, or infection supervenes, urination becomes painful as well as difficult Voluntary retention of urine or exposure to cold and wet may bring on acute and complete retention of urine as the first symptom Acute complete retention of urine is the first symptom of importance in almost half the cases. Loss of urine may be associated with, may precede or follow acute retention

True incontinence of urine does not occur as the result of prostatism. The loss of urine that does occur is overflow from the atonic, distended bladder The overflow of urine is the result of an irritation of the bladder; the loss of urine is involuntary

Hematuria is common from prostatism, and the presence of blood in urine is not necessarily indicative of the presence of malignant disease. The bleeding is usually due to an ulceration of the middle lobe, to acute inflammation, or perhaps to stone in the bladder Bleeding unavoidably occurs from the passage of instruments

Debility and age are the potent forces which annul the sexual powers Such a loss of function is not due to prostatism The congested prostate may excite abnormal erections which may be interpreted by an atherosclerotic brain as the return of youth and vigor which may lead the patient to the altar of marriage and soon thereafter to disaster

In some aging men an uninfected bladder may reach chronic distention with back pressure extending upward and involving the kidneys before there is known serious trouble. Under such circumstances the first symptom recognized is a loss of weight ... tipation and dry mouth This evidence may be

... r sooner or later in every case and are often initiated by catheterization The cystitis often follows even necessary catheterization The acute cystitis which follows the passage of a catheter begins acutely, often with a chill Spontaneous cystitis is often mild and superficial and may not cause pain or frequency of urination Spontaneous infection rarely, if ever, occurs before the use of the catheter or massage of the prostate for the chronic prostatitis which is present in every instance of infection.

Epididymitis may occur spontaneously or may follow instrumentation Often epididymitis is a symptomless chronic induration at one end of the epididymis Epididymitis may be severe ...

Seminal vesiculitis

The course of the d

vesicoureterorenal reflux of urine. The symptoms of the vesicoureterorenal reflux

Stenosis of the Neck of the Bladder. Stenosis of the vesical neck often is *congenital.* It may become manifest at any age. In infancy the bladder is so vigorous that it dilates with little sacculation in comparison to the megaloureter that ensues. In early life and up to 50 years of age the result of sclerotic obstruction is often diverticularization of the bladder and somewhat less dilatation of the ureter.

Stenosis, whether in the prostate or in the vesical neck, cannot be dismissed with the statement that it is due to inflammation, for gonorrheal urethritis and prostatitis are rarely followed by sclerosis sufficient to obstruct the neck of the bladder. Prostatic abscess rarely results in sclerosis.

Stenosis is commonest between the ages of 30 and 50 years, 20 years or so before the age of maximal incidence of prostatic hypertrophy.

The lesion of the vesical neck comprises chronic inflammation and sclerosis which involve the mucosa, the underlying tissues and the sphincter, often a secondary hypertrophy of the musculature of the bladder follows. The result of such sclerosis is achalasia, rigidity of the vesical neck.

SYMPTOMS. In most instances sclerosis of the neck of the bladder does not cause significant symptoms. Every severe posterior urethritis leaves some scarring about the vesical neck. These scars are not clinically sclerosis until there is retention of urine. The stream loses much of its force; the residuum is constantly at least 50 ml. The urinary stream is slow and small, difficult to start and ends with the dribbling of urine. There is nocturia.

EXAMINATION. Routine examination of the abdomen of a debilitated child may reveal a distended, palpable bladder which indicates the need for a urologic investigation.

Young men affected by stenosis of the neck of the bladder often have been embarrassed when they were boys by being unable to participate in micturition contests and, like girls, by having to urinate in the squatting position.

When the age is attained in which the prostate gland may become hypertrophied, if there is any sclerosis of the vesical neck, symptoms will be more intense and will occur earlier. The symptoms of sclerosis may be overshadowed if there is considerable general hypertrophy. The patient often has achalasia and sclerotic lateral intra-urethral lobes, which give the symptoms common to prostatism.

In *traumatic sclerosis* as the result of external trauma the urethra may be ruptured, for instance, as a complication of a fracture of the pelvis. The more familiar form of traumatic sclerosis, however, is that which follows prostatectomy or resection. After prostatic resection the onset of the lesion cannot be predicted. It may appear, causing retention of urine, before the patient has left the hospital. Symptoms rarely occur, however, before several years have passed.

DIAGNOSIS. The sclerotic bladder, on endoscopic examination, is almost always inflamed and edematous, cystic or ulcerated. Only the well-trained urologist can distinguish the constricting effect of achalasia from the spasm of inflammation and estimate its degree. Also, an expert, and only an expert, by cystometric examination can distinguish the neurogenic atony such as is observed in tabes dorsalis from the muscular atony of the bladder due to sclerosis.

Uncomplicated sclerosis of the neck of the bladder is suspected whenever retention of urine in the bladder is found and rectal touch reveals no enlargement or irregularities in the prostate. A small residuum of urine in the bladder of a patient who has arteriosclerosis and who is neurotic or psychotic does not interfere with the force of the urinary stream.

Hypertrophy of the Prostate. There may be a general hypertrophy of the prostate without significant obstruction to the flow of urine. The syndrome of prostatism depends on either the degree of sclerosis of the neck of the bladder or the presence of hypertrophy of the prostate in the neighborhood of the urethra. The amount of residual urine bears no essential relation to the size of the hypertrophy

partial or complete paralysis of the bladder. The absent ankle jerk is common enough in old age, yet when this sign is noted accompanied with the absence of deep muscle sense, the spinal fluid should be examined.

The prognosis of prostatic retention depends on the patient's age and on the character of the prostatic enlargement.

Tumors of the Prostate Gland. ***Benign Tumors.*** Occasionally *fibromas* and *adenomas* are discovered in the prostate. These usually present the symptoms of benign hypertrophy of the gland

Cysts of the prostate are usually single and apparently due to occlusion of one of the ducts. The cyst may project toward the urethra or the bladder or from the posterior surface or upper border of the gland Intra-urethral cysts grow large enough to cause complete retention of urine Retrovesical prostatic cysts grow to enormous size but do not cause symptoms except from their size.

The intra-urethral cysts usually project characteristically from the upper portion of a lateral lobe. Their translucency may be appreciated on cystoscopic examination

Malignant Tumors. CARCINOMA Cancer of the prostate is present in 1 of every 5 patients who have prostatism Prostatic cancer arises from the epithelium in the terminal acini of the ducts as a single focus or as multiple foci. The disease may remain confined to the gland for a long time Finally, however, the basement membrane is perforated and the neoplastic process passes into the lymphatic structures

The structural type of prostatic carcinoma varies widely. The highly malignant tumors are nearly all highly anaplastic They arise in prostates which have not been the seat of prior disease The tumors are small, regular in outline, and elastic. The lymphatics are invaded uniformly and the small veins are thrombosed early by tumor. There is immediate and widespread metastasis to the bones which may be the first evidence of the disease

The more definite adenocarcinomas are less highly malignant than those characterized by a high degree of anaplasia They invade the stroma more slowly but produce small, very hard, irregular tumors. The lymphatics in the organ are invaded, and metastasis to the regional lymph nodes occurs early in the disease There is a high incidence of perineal, sacral and sciatic pain Some adenocarcinomas may arise in large glands which are often of soft texture Demonstrable metastasis is rare. The true nature of the process is often not discovered until histologic study is made.

Metastasis of carcinoma of the prostate occurs mainly through the lymph vessels. The lymph vessels of the prostate are distributed with the internal iliac vessels and drain to the lumbar lymph nodes, which are continuous with the mediastinal lymph vessels and nodes In the lumbar region the nodes are in close apposition to the vertebrae, so that metastasis to the vertebrae is likely a retrograde extension In the highly malignant tumors the left supraclavicular lymph node is enlarged

Direct extension of the cancerous process into the perineural lymphatics in the prostate gland involves the sciatic plexus and gives rise to sciatic pain Bilateral sciatica in middle-aged men often suggests cancer of the prostate Metastasis less frequently involves the parenchyma of the lungs or liver The process in bone is at first destructive, later there is osteoplasia The deposition of calcium at the periphery of the tumorous deposit gives rise to the roentgenologic findings described as osteoplastic metastasis In some cases the osseous process is wholly destructive and remains so

The initial *symptoms* of cancer of the prostate comprise the urinary symptoms and pain The common urinary symptoms are frequency and difficulty of urination Other symptoms associated with these are nocturia, hematuria, urgency and incontinence Pain accompanying urination, backache, sciatica, or pain in the perineum, rectum or penis may be the cause for the patient to consult a physician

Occasionally, and usually when the tumor is highly malignant, urinary symptoms do not occur, even in well-advanced cancer of the prostate. When present, the

are the same as those of the urethral chill, but of longer duration. The renal infection usually becomes chronic. Pyelonephritis *may not be present, but if present it* may remain slight for years or may soon be complicated by hydronephrosis or may develop into pyonephrosis.

An occasional patient who has prostatism may have a stone in the bladder Stones may be present in those who have but little retention. If removed, stone will recur repeatedly until the prostate is resected.

Examination in Prostatism. A general physical examination is essential for disclosing the effects of prostatism and for determining other disease which is often present. An oval mass above the pubes, palpable bimanually, is a distended bladder. An irregular mass above the pubes may be a carcinoma of the prostate extending around the bladder; an oval mass not palpable bimanually is probably a urachal cyst

The *rectal examination* should not be made until the bladder has been emptied. Observe the patient while he urinates Often there will be this sequence of events: start—stop—start, slow, small stream which ends with weak spurts of urine and finally dies away with dribbles and then drops of urine which trickle over the end of the penis and fall in a backward direction

With the patient leaning forward at a right angle, the examiner's finger is moved across the *prostate gland* The findings of this examination are described with regard to lobal enlargements, smoothness and mobility An enlargement of the lateral lobes is manifested by bulging into the rectum. If the lateral lobes are widely separated, there may be enlargement intravesically, if close together, the enlargement may be intra-urethral. The hypertrophied lobes are usually symmetric, tense and smooth Irregularities felt on or in a lobe may be due to stone, inflammation or carcinoma. The benign prostate is relatively movable, the malignant tends to become fixed, owing to the periprostatic extension of the disease.

The *contraindications to catheterization* are (1) complete retention with distention and (2) acute infection of the prostate and fever Catheterization of a patient who has complete retention with a distended bladder palpable above the pubes is deferred until the patient is in hospital, prepared for decompression.

As the patient urinates, the sluggishness of the stream is noted If there is complete retention, the patient should be sent to hospital for decompression before further examination is made, though if the retention is acute, the bladder may be emptied at once by catheter If the patient has not been catheterized before, a rubber instrument is passed with gentleness, for it is this first catheterization that often infects the patient and may result in serious illness and death. The amount of residual urine is measured.

In the presence of small and even of medium-sized enlargements cystoscopic examination is often necessary in order to search for prostatic bar, diverticulum and tumor

If the patient is to be operated on and is not to be examined cystoscopically, an *excretory pyelogram* is made in order to detect unsuspected urinary stones and functional or anatomic defects in the kidneys. Concentration of urea in the blood is determined and often blood grouping and Rh factors are determined.

Diagnosis of Prostatism. The diagnosis of prostatism is made by the summation of the findings on examination which have been enumerated. Nocturnal polyuria of nephritic or of arteriosclerotic origin is often confusing and is differentiated so that a precise diagnosis of prostatic hypertrophy can be made Renal insufficiency

Tabes dorsalis cannot be distinguished either by the serologic [illegible] absence of knee jerk alone. The Argyll Robertson pupil is often diagnostically helpful. The absence of ankle jerk in association with a loss of deep muscular sense may be the only outward sign of tabes that is early, yet sufficiently ad[illegible] cause

It is realized that regions of increased circumscribed hardness situated within the prostate gland are not pathognomonic of cancer. Such nodules may be due to stone, chronic disease, tuberculosis or chronic prostatitis.

SARCOMA. Sarcoma of the prostate is a highly malignant tumor of connective tissue origin which usually occurs only in infants and children; its rate of growth is extremely rapid, it metastasizes readily to the lungs and is frequently fatal within a few months of its onset. The symptoms which it produces are purely obstructive, complete retention following rapidly the increased difficulty in urination Rectal examination reveals the presence of the large elastic mass which has replaced the prostate Up to date, sarcoma of the prostate has been uniformly fatal and the only available treatment is palliative.

THE PELVIS

The male pelvis is fashioned pre-eminently for locomotion it is both heavier and rougher than the female pelvis The female pelvis, in addition to the functions of locomotion, has the added function of gestation. The cavity of the female pelvis is larger and shallower than that of the male pelvis It is smoother, its bony prominences are less conspicuous. The symphysis pubis is narrower and the sacrum is shorter and less curved The acetabula are set wider apart

Pelvic Hernias. Hernial protrusions of the pelvic contents may occur through the upper portion of the obturator membrane, following the vessels and nerve. Such a protrusion is called an obturator hernia It makes its appearance in Scarpa's triangle and is covered by the pectineus muscle Sciatic hernia is the name given to those forms in which the intestine escapes through the great sciatic notch, passing just above or just below the pyriformis muscle Perineal hernias may push down between the rectum and bladder and bulge in the perineum. They may pass between the coccygeus and levator ani muscles or between the fibers of the latter and bulge into the ischiorectal fossa or forward into the labium of the female

Pain in the External Genitalia. The *labia majora and minora, clitoris, vestibule and urethral meatus* are sensitive to heat, cold and touch. The skin of the labia majora is more sensitive than the skin or the mucous membrane of the labia minora to heat, cold, touch or pinching.

The *urethras* of both men and women before instrumentation are usually sensitive, whereas a much instrumented urethra in either sex may become insensitive Gentleness, persuasion, and reassurance to induce relaxation before and during instrumentation may overcome much of the apparent sensitiveness. The pain elicited by instrumentation of the urethra is due in part to the sudden stretching of a contracted muscle, rather than to the sensitivity of the mucous membrane The passage of the cystoscope may elicit a desire to defecate

Overdistention of the bladder with solutions at any safe temperature produces first a feeling of fullness and then of pain in the suprapubic region and in the urethra, associated with an intense desire to urinate The pain from overdistention of the bladder in men is referred to the end of the penis In women the pain from overdistention is referred to the labia minora and clitoris.

Pain from stimulation of a *ureter* may be felt ipsilaterally, and its location in the skin follows approximately a line drawn along the lateral edge of the rectus muscle. The area of the cutaneous site of pain may be hyperalgesic as tested by pin prick.

When the *ureterovesical junction* and the first 2 inches (5 cm.) of the ureter are distended or stimulated, pain may be felt in the suprapubic region along the urethra and is accompanied by an intense desire to urinate. In some instances the pain extends from the suprapubic region up the midline of the abdomen as far as the umbilicus and may spread across the abdomen In an occasional individual stimulation of the ureter may cause pain along the anterior surface of the thigh and leg to the knee.

Dilatation of the normal *renal pelvis* always elicits pain that is felt in the costovertebral angle There is no recognition of heat or cold sensation in either the renal pelvis

symptoms of urinary difficulties and pain become more severe as the disease progresses.

On *rectal examination* there may be an irregularity of the contour of the prostate or differences in density in various parts of the gland. In advanced prostatic cancer there is an extension of the hard irregular infiltration beyond the confines of the organ, about the base of the bladder and the seminal vesicles, fixing the organ in the pelvis. If there is a large and hard single nodule confined to the organ, it may be due to the presence of stone. Multiple small calculi may produce crepitus when pressure is brought to bear by the examining finger.

Cystoscopic and endoscopic examinations are of little value in early cancer of the prostate The residual urine is measured, and this too is variable. Roentgenologic examination of the bony pelvis and lower lumbar vertebrae will often reveal the presence or absence of metastasis to the bone or the presence of stone in the prostate.

The changes in the values of the acid and alkaline phosphatase in the blood may be of great aid in detecting metastatic lesions in the bone not yet visible by roentgenologic examination

Acid phosphatase is an enzyme which is found in the epithelial cells of the prostate gland in sexually active men and in the cells of prostatic cancer. Values of more than 10 Bodansky units per 100 ml of serum are significant. Normally there is a small amount (less than 3 Bodansky units) of this substance in the blood serum The enzyme owes its existence to the sustaining influence of the male sex hormone After castration it disappears from the prostatic epithelium, and a coincidental shrinkage of the tissues ensues

It is well established that sustained elevation in the serum acid phosphatase level occurs when malignant metastasis has involved the bone marrow and lymph nodes Investigations have shown that transient elevations in the serum titer of this enzyme may be detected after the trauma of operation on the prostate gland and subsequent to digital manipulation, but not as the result of prostatitis, benign prostatic hypertrophy or tumor metastatic to the prostate from other organic structures. Thus sustained abnormal elevations of this enzyme are pathognomonic of metastatic prostatic carcinoma

Alkaline phosphatase is produced by bone as an essential agent for growth and repair The normal values are 1 5 to 4 Bodansky units per 100 ml of serum in adults, and 5 to 14 units per 100 ml of serum in children With few exceptions its serum level reflects bone activity in the absence of hepatic disease. However, in the presence of known metastatic prostatic carcinoma its elevation may signify osteoblastic response to invading tumor and thus serves as an index of the extent of such activity When elevations are present in cancer of the prostate gland, the serum level of the alkaline phosphatase is generally higher than that of the acid phosphatase After castration, when remission occurs, the acid phosphatase level promptly drops to normal, whereas there is a temporary rise in the alkaline phosphatase value, followed later by a drop toward the normal level This behavior affords an index of the effectiveness of treatment

The presence of an abnormal serum acid phosphatase level in the absence of evident metastasis in a patient who has prostatic cancer implies a poor prognosis The presence of a normal serum acid phosphatase value in a patient who has metastatic prostatic carcinoma does not necessarily imply poor response to endocrine therapy. Serum alkaline phosphatase concentration is not in itself specific for prostatic carcinomatous activity without metastasis to the bone.

The *diagnosis* of cancer of the prostate is never certain until biopsy is made at the time of operation. In the presence of urinary difficulties, metastasis to bone and sciatic or perineal pain suggest the diagnosis of cancer of the prostate Add to this a hard, fixed prostate gland on rectal examination and the diagnosis is almost conclusive.

Primary carcinoma of the prostate must be differentiated from secondary carcinoma metastatic from some other primary lesion, particularly rectal carcinoma, and from sarcoma, prostatic cyst, and tumors of the rectum, sigmoid and base of the bladder as well as from the more usual prostatic lesions

broad ligament Cysts arising from Gartner's duct are sometimes found in the vagina. In the male, cysts arising from the wolffian duct are (1) encysted hydrocele of the testicle and (2) general cystic disease of the testicle. Cysts arising from the persistence in the male of Muller's duct have also been observed in the prostate and seminal vesicles, but they are exceedingly rare

This discussion is continued with the description of the disease of each organ.

THE EXTERNAL FEMALE GENITALIA

The labia majora meet anteriorly in the anterior commissure and posteriorly in the posterior commissure They vary greatly in size and in color; often the median sides of the labia are very much more pigmented than the surrounding skin. The space between the posterior commissure and the anus, about 1¼ inches (3.2 cm.), is the perineum.

The labia minora divide anteriorly to form the prepuce above the clitoris and the frenum on its lower surface Posteriorly they decrease in size to a thin crescentic fold of mucous membrane called the fourchet. Like the labia majora, the labia minora vary greatly in size and particularly in the anteroposterior width They often project outside of the labia majora The space between the labia minora is the vestibule. The meatus or urethra is in the vestibule 1 inch (2.5 cm.) behind the clitoris It is surrounded by a ring of mucous membrane, and when a catheter is to be introduced, the urethra can be seen by separating the labia minora, or it can be recognized by the sense of touch The openings of the para-urethral ducts are just below and to the outside of the meatus The vulvovaginal glands (of Bartholin) empty on the inner side of the labia minora in the sulci between them and the hymen.

The hymen partly occludes the lower end of the vagina across its posterior portion The carunculae hymenales are the remains of the ruptured hymen. The fossa navicularis is the space between the hymen and the fourchet.

THE VULVA

The vulva includes the mons veneris, labia majora, labia minora, clitoris and prepuce, vestibule, hymen, urethral meatus and Bartholin's and Skene's glands. Variations in size and true hypertrophies of the clitoris and labia minora are common In rare instances there may be a complete double vulva

The vulva becomes edematous when there is edema of the extremities as in congestive heart failure. Varicosities of the vulva may be associated with varicose veins of the legs Hematomas occur in the normal vulva after trauma. They may become large and painful

Acute Vulvitis. Acute nonvenereal vulvitis includes intertrigo, a diffuse reddening of the skin of the vulva and folds of the thigh, which occurs in infants and obese women, mainly during hot weather Follicular vulvitis or hair follicle infection is common Furunculosis or boils may develop in hair follicles Noma, a gangrenous vulvitis in young girls in tropical climates, follows severe systemic infections such [illegible] The diabetic [illegible] itis

[illegible] Bartholin's and Skene's glands, is not ordinarily involved in gonococcal infections, and the majority of th[illegible]

[illegible] is occasionally seen [illegible] is common in children The vagina is inflamed and there may be redness and swelling of the vulva.

Weaver stresses the value of bacteriologic cultures in the detection of the gonococcus in contrast to the inadequacy of the stained smear, pointing out that in known

or the ureters. Lennander observed that the outer surface of the kidney could be pinched, cut, or have heat and cold applied without eliciting any sensation.

Distention of the right renal pelvis may produce pain *extending down toward the* right groin, and sometimes spreading to the urethra and testicle Ockerblad and Carlson observed that faradic stimulation *within the renal pelvis* always elicited pain which was felt on the back at the costovertebral angle and that the pain never extended around to the front, nor upward from this point.

THE FEMALE GENITALIA

Aberrations of the Female Genitalia and Their Correlations with Homologous Structures in the Male. The wolffian duct with a collection of tubules is known as the wolffian body, and reaches its full development in the seventh week. On one side of the wolffian body develops the sexual gland, which later becomes in the male a testicle, in the female an ovary By the end of the second month the kidney develops at the caudate extremity of the wolffian body. At this time the bladder is connected by the urachus with the stalk of the allantois The lower end of the bladder is connected with the extremity of the intestinal tract through a dilatation called the urogenital sinus The union of the *urogenital sinus and intestine forms the cloaca At the time the* wolffian body is developing, there appears alongside of it a tube called Muller's duct This duct atrophies in the male but in the female becomes the uterine tube, uterus and vagina. The ureter is developed and becomes connected with the lower portion of the bladder.

The wolffian duct and the mullerian duct, until about the third month, empty into the urogenital sinus. Differentiation of the sexes begins about the third month and is well advanced in the fifth. As stated, the sexual gland in the male becomes the testicle, and passing from its lower end is seen the gubernaculum In the female the sexual gland becomes the ovary, and the round ligament passes from its lower end The wolffian body, after performing temporarily the functions of a kidney, disappears, leaving sometimes a small cyst, known as the hydatid of Morgagni (stalked hydatid), attached to the upper part of the epididymis in the male and in the broad ligament near the ovary in the female In the lower portion of the hydatid are the remains of the wolffian body comprising some short closed tubes in the tail of the epididymis known as the paradidymis or organ of Giraldès in the male, and the paroophoron of the broad ligament *in the female The wolffian duct, which forms the vas deferens and part of the* epididymis in the male, forms the atrophied paroophoron in the female to the inner side of the ovary.

The parovarium or organ of Rosenmuller is the remains of the middle set of wolffian tubules and in the male forms the epididymis In the female it is almost always present as a horizontal tube with shorter tubes connected with it, between the layers of the broad ligament near the ovary The wolffian duct may persist as a small tube, known as the duct of Gartner, in the broad ligament close to the uterus and vagina In the male the mullerian ducts atrophy and form the sinus pocularis of the prostate Part of them may persist patulous as Rathke's duct As stated, in the female they form the uterine tubes, uterus and vagina

Exstrophy of the bladder, epispadias, hypospadias and *various forms of* hermaphroditism result when the walls of the bladder and urethra and external genitals fail to develop in the median line Should the urachus not close, a fistulous tract leads from the bladder to the umbilicus from which urine discharges Cysts may also form in its course If the partition between the rectum and the anus is not absorbed, there is formed *one of the varieties of imperforate anus. In some cases* the rectum empties into the urethra or bladder, thus forming a cloaca Should the testicle become arrested in its descent from the region of the kidney, it forms what is known as undescended testicle It may be arrested within the abdominal cavity, in the inguinal canal, or near the external abdominal ring.

The paroophoron *gives rise to cysts which have a tendency* to develop between the layers of the broad ligament and are papillomatous inside. The parovarium also gives rise to cysts which likewise tend to burrow between the layers of the

The lesion may occur on other portions of the skin such as the face, neck, and back. Often the gross appearance is most characteristic.

The diagnosis is based on the results of examination of scrapings from the ulcer stained with Wright's stain or Giemsa's stain; the presence of Donovan bodies (Donovania granulomatis) as clusters of cocci, some occurring particularly in large endothelial cells, but also in monocytes, leukocytes, and in clusters outside of cells partially contained in a membrane, has been accepted as diagnostic Some of the organisms are surrounded by thick, dark capsules All other venereal diseases must be ruled out by serologic examinations and skin tests.

Lymphopathia Venereum and Psittacosis Viruses. Synonyms for lymphopathia venereum are climatic bubo, tropical bubo, venereal bubo, fourth venereal disease, sixth venereal disease, lymphogranuloma inguinale, granulomatous lymphomatosis, poradenitis, esthiomene, and maladie de Nicolas et Favre.

Lymphopathia venereum is a protean disease usually transmitted by venereal contact, and manifested by both constitutional symptoms and acute and chronic tissue changes in the inguinal and anorectal regions. It is caused by a virus which is similar to that which produces psittacosis.

In the first stage it forms a superficial ulcer which varies from a few millimeters to ⅘ inch (2 cm) in diameter This primary lesion may occur at any point in the vestibule or inner surfaces of the labia, commonly on the urethra or in the fourchet. It may disappear soon or may develop into a deep lesion on the vulva or on the sides of the vaginal orifice, completely destroying the urethra. If the primary lesion occurs on the upper two thirds of the vulva, the lymphatics drain to the inguinal lymph nodes, with formation of bubo and perhaps multiple draining sinuses Not infrequently the lymphatic channels of the vulva are blocked, forming elephantiasis, chronic hypertrophic vulvitis or esthiomene Inguinal involvement in women is less common and less severe than in men If the virus involves the urethra, ulceration and strictures may follow Because of the lymphatic drainage from the primary lesion, rectal strictures are commoner in women than in men. Diagnosis of the late lesions may be fairly accurate from the gross appearance, but should be substantiated by exclusion of other lesions.

Lymphopathia venereum must be differentiated from chancroid, bubo due to pyogenic lesions of the lower extremities, tuberculosis of the inguinal lymph nodes, gonorrhea, syphilis, granuloma inguinale, balanitis, plague, tularemia, carcinoma and tuberculosis of the rectum, and ulcerative colitis Films of pus or biopsy material are examined for elementary bodies by means of the Macchiavello stain *Suspected material should be inoculated intracerebrally into mice.* The serologic tests for syphilis, Ducrey's skin test, darkfield, smears, scrapings, and biopsy and the Frei test all are performed as parts of the differential diagnosis.

The Frei test consists of the intradermal injection of 0.1 ml of antigen and 0 1 ml. of control material Results of the test are read 48 to 96 hours after injection, and, if the reaction is positive, the central induration of the papule caused by the antigen measures 6 by 6 mm or more, while that caused by the control material measures 5 by 5 mm or less

Reaction to the Frei test usually becomes positive 7 to 40 days after the onset of the adenitis Negative reactions in definite cases are rare, they are usually due to such factors as the menses, septicemia, fever, tuberculosis, and coexistent early syphilis or early chancroid

Axelrod tested the yolk sac virus antigen of venereal lymphogranuloma and found that the results of the virus antigen are consistent with positive history and signs of the disease. This test has not come into wide clinical use Bedson and co-workers demonstrated that titers of 1 32 or more in the complement fixation test made with steamed virus of lymphogranuloma venereum and the serum samples from patients in whom the clinical observations are compatible with a diagnosis of lymphogranuloma venereum

cases of gonorrhea in women gram-negative diplococci may be found in stained smears in less than 20 per cent of the cases, whereas cultures on proteose peptone hemoglobin agar yield a correct diagnosis in more than 75 per cent. At Weaver's laboratory, when oxidase-positve gram-negative diplococci are found on cultures, they are further studied from the standpoint of their fermentation reactions on various sugars The gonococci will ferment glucose but none of the other sugars *Neisseria sicca* ferments all the sugars except mannitol It is this organism to which Weaver calls special attention, because physicians who depend on staining procedures for the diagnosis may make false positive diagnoses

Syphilis. A chancre is often situated near the vaginal orifice on a labium majus or minus or about the rectum. It is a grayish, granular ulcer, round or oval, from ⅖ to ⅘ inch (1 to 2 cm) in diameter, raised, flat and firm Multiple chancres occur in the folds where the labia are in contact. The diagnosis is proved by darkfield examination, demonstrating the spirochetes.

Secondary lesions occur as condylomata lata and mucous patches. The tertiary lesion forms deep crater-like ulcerations Diagnosis is suggested by results of the histologic examination and disappearance of the lesion under antisyphilitic therapy. Positive results of serologic tests are present when the lesions are secondary and tertiary, but by no means are these diagnostic of vulval syphilis. Tertiary syphilitic manifestations originate extremely infrequently in the vagina. The isolated submucous gumma breaks down early and appears in the form of a characteristic ulcer.

Granuloma Inguinale. There are three infections of the anorectal regions and external genitalia of both men and women which are characterized by ulcerations and inguinal lymph-node involvement, ulceration of the skin or mucous membranes, and often abscess formation These are (1) granuloma inguinale, (2) lymphopathia venereum and (3) soft chancre (see also page 410)

Granuloma inguinale is a bacterial disease, the exact causative bacterium is unknown Lymphopathia venereum is a viral disease, and soft chancre is caused by *Hemophilus ducreyi*

Granuloma inguinale originates from the organisms which produce Donovania granulomatis The disease is largely limited to Negroes or to persons of mixed race who have Negro blood Granuloma inguinale or granuloma venereum or pudendal ulcer is primarily a disease of the skin, producing an ulceration which has a tendency to extend from the vulva to the inguinal regions.

Packer, Turner and Dulaney called attention to the fact that the earlier concepts of the progress of this infection solely by serpiginous spread or by auto-inoculation have been broadened in recent years as a result of accumulated evidence of lymphatic spread and involvement To lymphatic spread has also been attributed the extensive involvement of the pelvic organs following granuloma inguinale of the cervix and vagina Of significance are the pronounced systemic manifestations which are frequently associated with lesions in this region, particularly when complicated by pregnancy These systemic manifestations indicate that granuloma inguinale, far from being strictly a local disease of the genitalia, has potentialities for widespread dissemination throughout the body, either of the specific etiologic agent or of the products of secondary invaders The former possibility has already been demonstrated by a few reported cases of metastatic lesions of bones and joints in distant parts of the body following lesions of the genitalia Thus has evolved from the early beliefs of the limited implications of this disease a clearer understanding of the possibilities for widespread dissemination which the disease possesses

The initial lesion begins as a papule ⅕ to 1⅔ inches (1 to 4 2 cm.) in diameter, develops into an ulcer, and may denude the skin of the vulva, perineum and gluteal folds. The cutaneous margin of the ulcer is raised and pigmented and has a serpiginous border and a bright pinkish red granular-appearing base which reflects light

glands. These lesions may itch. Urine may be a constant cause of irritation and burning

Collections of smegma round the clitoris or in the folds between the labia are prone to produce irritation and mild itching sensations. A persistent and irritated hymen, everted vaginal mucosa due to relaxed vaginal outlet, gonorrheal warts, leukoplakia, vulvitis, and ulcerative or neoplastic diseases of the vagina or external genitalia all may cause itching.

Protective pads or intravaginal tampons used to absorb menstrual and leukorrheal secretions may be responsible for irritations and itching. Dermatologic factors include infections of the hair follicles and sweat glands, fissures in the skin, dry scaly dermatitis in which the skin becomes diffusely irritated, reddened, purplish or grayish and appearing as if it had been scalded. A rare form of pruritus is itching which involves the fossa navicularis, vestibule or interior of the vagina

Vaginismus. This is a painful spasm of the vagina due to local hyperesthesia. Vaginismus is termed superficial when the discomfort is at the entrance of the vagina. It is termed deep when the discomfort is situated deep and seemingly in the bulbocavernosus or in the levator ani muscles. In some instances the discomfort is apparently due to spasm of the constrictor vaginae muscle Vaginismus is termed psychic when there is extreme aversion to coitus The act is attended apparently by painful contraction of all of the muscles of the vagina

Nymphomania. The term nymphomania is employed to designate an exaggerated sexual desire in a woman It is a condition the opposite of vaginismus and, like the psychic form of vaginismus, it has nothing to do with the state of physical health or the hormones of the glands of internal secretion These women often have had abnormal sexual experiences and frustrations This condition is often present as a part of schizophrenic psychosis

On examination the labia are large and have a rugged appearance and may be excessively pigmented

Leukoplakia Vulvae. The term leukoplakia vulvae refers to areas of thickening on the skin The cause of leukoplakia is unknown The disease is characterized by translucent white patches of irregular size which may have indefinite borders or may be widespread It occurs particularly about the clitoris, labia minora, and on the perineum It may occur inside the rectum Very commonly there is associated kraurosis Pruritus is common and severe Lichen planus and leukoplakia bear a great resemblance to each other when situated on the vulva In lichen planus similar lesions will be present on the flexor aspects of the forearms, fronts of the legs and perhaps in the mouth

In the differential diagnosis lichen planus is to be excluded Lichenification is differentiated by the fact that it commonly follows protracted pruritus. The spots of lichenification are thickened, diffuse, usually symmetric, situated more on the outer parts of the labia majora and between the buttocks round the anus than elsewhere. Lichenification is usually moist and has fissures

Leukoplakia represents a truly premalignant lesion

Tumors of the Vulva. *Benign Tumors.* *Condyloma acuminatum* (verruca acuminata), or venereal wart, is often the result of unsanitary conditions Warts of this type are common in the obese, during pregnancy, and in association with gonorrhea

Verrucae acuminatae occur on the vulva, in the vagina and urethra and on the cervix. They may be a few millimeters in diameter or a cauliflower mass that almost covers the external genitals They are distinguished from the flat, sessile condylomata lata

Fibromas and *fibrolipomas* of the vulva are common. The fibroma is hard and movable and is covered by healthy skin. It is usually small. The fibrolipoma is

suggest active infection with the virus of lymphogranuloma venereum. The serums from human infections with the viruses of psittacosis and lymphogranuloma venereum show a high degree of cross reaction in the complement fixation test with antigens made from these two viruses. The Frei test also merely indicates that infection with a virus of the lymphogranuloma venereum and psittacosis group has occurred A positive reaction to a Frei test together with a positive reaction to a complement fixation test at a serum dilution of 1 . 16 or more in a patient suspected of having lymphogranuloma venereum is good evidence of active infection with the disease Acid extracts of lymphogranuloma venereum and psittacosis viruses appear to give specific reactions when injected intradermally in human infections with these two viruses

Herpes. Herpes genitalis in women is due to the herpes simplex group of viruses which affect the mouth and nose, and the male genitalia Bullous lesions may occur singly or multiply or extensively. Ordinarily, however, a single vesicle, followed by an ulcer, appears about the labium or the vaginal orifice.

The blisters may break and form numerous small superficial tender ulcers. At times it has been thought that herpes is transmitted by sexual intercourse, but it often occurs without intercourse Occasionally the ulcers recur with each menstrual period In such cases the diagnosis is not difficult. Smallpox vaccine has been used for treatment with some success

Ecthyma of the Vulva. Ecthyma of the vulva resembles condyloma latum. The lesions begin as pustules and form depressed ulcerations. *Staphylococcus aureus* and *Streptococcus pyogenes* may be cultured.

Kraurosis Vulvae. In kraurosis vulvae the skin is white, red or mottled and appears dry and thin There is a progressive shrinkage of the vaginal orifice, labia minora and clitoris, and of the labia majora. The mucosal border seems to extend beyond the normal confines and has a smooth glistening unhealthy appearance Kraurosis is common after the menopause Pruritus may be associated, with secondary infection incident to injury of the skin from scratching. Inflammatory ulcerations are slow in healing, mainly because of persistent irritation

Disease of the Vulva Due to Disturbances of Innervation or to Absence of Psychic Control. ***Pruritus Vulvae.*** Intense itching is a symptom of various skin diseases and may occur idiopathically as a neurosis. Itching may be an undesirable normal impulse, for it is present in varying degrees each day in every man, woman and child. If judgment can be rendered from observations of them scratching or making various rubbing movements as substitutes for scratching, all mammals are likewise troubled almost constantly by itching about the anus and genitalia

In women genital and perineal pruritus is common and is perhaps the most disabling form of pruritus It may be temporary and insignificant, such as the itching that is often felt during menstruation; on the other hand, it may become a fixed obsession. The irrepressible impulse to scratch creates a vicious cycle, for scratching makes itching As an obsession a pruritus gives its victim very little rest or peace, and eventually there is present a deterioration of the disposition and health

Senile and atrophic changes in the skin, due to a normal or artificial menopause or irradiation therapy, are frequently accompanied by pruritus. In these conditions the skin becomes thin and wrinkled, loses its resistance to infection, and becomes susceptible to irritation.

Pruritus ani and vulvae are common in obese women whose genitals are constantly wet with perspiration.

Rectal discharges and intestinal infections may cause pruritus Also disorders such as hemorrhoids, proctitis, parasitic intestinal infections, fissure and rectal polyps are frequently the basis of the trouble. Pruritus may be ascribed to diabetes mellitus. However, in practice the impression is gained that most instances of pruritus are not associated with diabetes.

In some cases pruritus starts as urethritis or as an infection of the periurethral

Urethritis. Urethritis is an inflammation of the mucous membrane of the urethra. It may be either acute or chronic.

ACUTE URETHRITIS. The female urethra is short and straight and has a wide caliber, and urethritis is therefore almost always a temporary condition. However, if the periurethral glands are involved, they may affect the urethra and bladder permanently Stricture of the urethra is not common in women

The chief symptom of urethritis is burning on urination. If there is frequency, one suspects some disorder (cystitis) within the urine-containing viscera There may be a constant burning or itching sensation.

On examination, in the acute stage, the urethral meatus is swollen and red, and pus can be expressed from its lumen. The infection usually involves also the submucous tissues and the periurethral ducts of Skene and any glands or congenital diverticula that may be situated along the urethral canal.

CHRONIC URETHRITIS Chronic urethritis in the female has no distinguishing features except for the exacerbations of the acute urethritis it originates.

On examination the urethra may feel thick and it is sensitive. The diagnosis is made by endoscopic examination In addition to the evidence for a chronic inflammation there are cystic changes in the urethral epithelium

Relaxation of the Vesical Sphincter. The vesical sphincter normally is sufficiently strong to hold urine under excitement, coughing, sneezing or lifting. It is a common experience in parous women that coughing will be accompanied by a loss of a few drops of urine. In man and other mammals excessive fear, fright or pain will be accompanied by a loss of urine This is called stress incontinence and is a normal act.

Stress incontinence of a marked degree may occur in virgins, neurotic men and nulliparous women In such instances it is due to an overreaction to which these individuals are subject. There is no organic disease of the urinary structures.

Childbirth Injuries of the Urethra. Childbirth injuries comprise urethrocele, relaxation of the vesical sphincter, and urethral fistulas

Urethrocele usually accompanies *cystocele*. It is a relaxation of the anterior vaginal wall in the region of the urethra. The symptoms are identical in both cases. Not infrequently a urethrocele remains after the cystocele has been repaired surgically unless the urethrocele is discovered and corrected at the same time. This may account for the persistence of symptoms after a cystocele has been surgically repaired

Urethral Obstruction. Urethral obstruction in women is uncommon It is unusual for a woman to have stricture of the urethra subsequent to gonorrhea or other infections

A urethral obstruction may be partial or complete, acute, or chronically slow in development depending on its cause

Partial obstruction occurs in middle-aged women as a sequel of chronic infections resulting from trauma of coitus, childbirth or, in elderly women, from senile changes in the mucous membrane. Unusual causes are extensive inflammatory lesions and tumors In middle-aged women the obstruction usually is situated in the outer third of the urethra or at the external orifice. The orifice is so small that a ureteral catheter is passed with difficulty

The symptoms of partial obstruction are difficult and slow urination, burning, frequency, urgency and pain There is often an associated recurring cystitis As soon as the urethra is completely cured, the cystitis usually disappears.

In the aged woman who has a small urethral orifice, normal functioning may be carried on for a long time The onset of any superimposed inflammatory reaction, however, soon causes enough edema to transform such a lesion into a complete obstruction

On examination the urethra is more rigid than normal and it feels indurated

usually softer, may be attached to the skin by fibrous bands, and is often lobulated Occasionally a fibrolipoma becomes pedunculated, and may attain large size.

Sebaceous cysts are common in the vulvar skin. Usually they are round or oval and project above the skin. Their characteristic appearance is a grayish color, the overlying skin being tense, adherent and thin. The whole tumor is freely movable

Sweat gland tumors (hidradenoma) are uncommon growths that originate in the sweat glands of the labia The tumors ordinarily are not more than ⅖ or ⅘ inch (1 or 2 cm) in diameter. They occur in older, or at least middle-aged, women The lesions are smooth and covered by normal skin, resembling small subcutaneous fibrolipomas or sebaceous cysts Openings in the overlying skin may suggest that the lesion is a sebaceous cyst. The histologic appearance may suggest adenocarcinoma

Malignant Tumors. *Carcinoma of the vulva* is primarily a disease of women past the menopause, although it occurs at times in younger women The average age of the patients is about 60 years These carcinomas are of the squamous cell variety arising from the skin at mucocutaneous borders. The lesions appear on the labia, on the clitoris or in the vestibule They often are associated with leukoplakia or with carcinoma of the rectum. They do not develop rapidly but ulcerate early The lesion becomes a nodular, weeping, putrid-smelling ulcerated mass It is diagnosed by biopsy and histologic examination

Adenocarcinomas of Bartholin's glands are rare. They appear as hard nodules beneath the skin in the region of the gland. Occasionally adenocarcinomas arise from the sweat glands. Secondary adenocarcinomas arising from the uterus or rectum form hard undermining ulcerations in the vulva Diagnosis is by histologic study of biopsied tissues.

Melanotic sarcoma and *sarcoma* on the vulva are rare

THE FEMALE URETHRA

The female urethra, 1⅗ to 2⅖ inches (4 to 6 cm.) long, leads from the vestibule to the bladder The external urethral orifice is usually situated about halfway between the clitoris and the anterior margin of the vaginal orifice

It is subjected to and may be injured by the discharges from the uterus and vagina, and may be contaminated by feces, especially in infants and in adults who have incompetent anal sphincters The urethra is easily traumatized in childbirth

Skene's ducts or glands open into the urethra immediately within the external meatus Other than Skene's glands, Cabot and Shoemaker observed only epithelial crypts and recesses which perhaps were the rudiments of embryonic glandular structures but not true urethral glands. Urethral diverticula are rare

Hypospadias. *The female urethral orifice normally is situated* well above the vaginal margin and is clearly visible However, it may occupy a lower position and open into the vagina This abnormality is due to arrested development of the urogenital sinus and to incomplete separation of the orifices of the urethra and vagina.

The extreme malformation is observed when the vagina opens into the *posterior* urethra This is seen only in the presence of gross malformation such as hermaphroditism.

Hypospadias *in* women rarely causes any notable symptoms Occasionally it may produce external irritation, especially on intercourse In some instances this condition favors the development and persistence of urethritis and cystitis

Infections of the Urethra. The urethra is often a portal of infection in girls during childhood. Skene's ducts *externally and some glands and epithelial* crypts in the posterior portion of the urethra may maintain infections and cause recurrences of cystitis. In women gonococcal infection in diverticula or in Skene's glands may be the focus of reinfection Glands along the posterior part of the urethra and even diverticula are difficult to discover on endoscopic examination

Urethrocele is a herniation through the urethrovaginal septum and not through the urethral meatus

THE INTERNAL FEMALE GENITAL ORGANS

EXAMINATION. The examination of the female genital organs is performed with the patient in any one of four positions It is assumed that the patient is fully undressed and that all unnecessary exposure is avoided

1 The routine examination is conducted with the patient lying on her back, on an appropriate examining table, with her knees flexed, and hips fully flexed, the thighs drawn up on the abdomen, and the coccyx lifted so as to lessen the inclination of the pelvis. The heels support the flexed legs on stirrups on the corners of the table, or the thighs are supported by leg holders or are held by assistants

2. A position especially valuable for examination of the portio vaginalis, the rectum and the bladder is the knee-chest position. The elbows and knees of the patient support the body The shoulder girdle is in a low position, while the back and buttocks are high. The abdominal and pelvis viscera fall toward the diaphragm, and the attachments of the pelvic organs are stretched.

3. To afford a better view of the cervix the patient lies on her left side with the left arm behind her and allows the right shoulder to sink as far forward or downward as possible, the abdomen and thorax resting on the table. The knees are flexed, and the thighs drawn up (Sims' position).

4 The standing posture is especially valuable if the patient has a descensus or other displacement of the pelvic organs For this examination have the patient stand with one foot on a low stool before the examiner In this posture the degree of descensus can be determined and the posterior and lateral walls of the pelvis can be thoroughly palpated.

It may occasionally be necessary to anesthetize the patient in order to relax the parts for examination, but the greater the experience of the physician, the less often will this method be required In young unmarried women a rectal examination will usually suffice

A pelvic examination is never performed without knowing that the bladder is empty For the examination of the female pelvis the index and middle fingers are used The hand may be covered with a rubber glove or the fingers covered with finger cots. The covered fingers are lubricated The fingers are introduced into the vagina if the outlet is marital If the outlet is virginal, only a rectal examination is made

Bimanual Examination After the preliminary examination of the vagina and cervix, the exact position of the *portio vaginalis* or *cervix* is ascertained Normally, when the uterus is in the position of anteversion, it lies behind the spinal line (connecting the spines of the ischia), the external orifice of the uterus, or os, being directed backward, and the anterior lip being longer than the posterior. The cervix should lie approximately in the median line.

Bimanually to palpate an anteverted *uterus*, the examiner places the fingers of one hand above the right pubic bone and presses gradually into the depth, while the fingers in the vagina, one finger on the anterior lip of the cervix, shove the tissues just in front of the cervix strongly upward. As soon as a resistance is felt by the external hand, the pressure of both hands may be slightly increased, when the body of the uterus can be felt between the two hands. Or, the fingers in the vagina may press forward from the posterior wall, in which event the portio vaginalis, along with the body of the uterus, is shoved against the external hand. Should the uterus lie abnormally high, it may be necessary to press with the fingers directly against the tip of the cervix in order satisfactorily to palpate the uterine body.

To make sure whether a resistance felt is really due to the body of the uterus, a test is made to ascertain whether the portio vaginalis, which is certainly a part of

Obstruction by extrinsic tumors is obvious. On direct endoscopic examination by one trained sufficiently to perform such an examination, the urethra is red and inflamed, the normal longitudinal striae are absent and the mucous membrane is injected. There may be hypertrophy of the bladder, as evidenced by a mucous membrane which is irregular, owing to trabeculations of the hypertrophied muscle and inflammation If overdistention and dilatation persist, hydronephrosis and impairment of renal functional activity ensues.

The diagnosis is made by inspection and palpation of the urethra and the passage of urethral sounds and dilators by skilled hands.

Incontinence. On occasion, in men, women and children, the bladder gradually becomes distended with urine because of some neurogenic or organic disturbance in the passage of urine so that it is never completely emptied When the bladder becomes distended to its full capacity and empties only by the pressure of the abdominal wall, the condition is called paradoxical incontinence. The overflow voiding may be practiced by the patient who learns that voiding may be accomplished by flexion or bending the body forward often while at stool. The amount of urine is normal, and frequency of urination occurs without intervening incontinence In these patients the full bladder on palpation simulates an abdominal tumor.

Enlargements and Tumors of the Urethral Meatus and Urethra. *Eversion* of the urethral mucosa is common in women because the boundary separating the mucosa of the urethral canal and the surrounding epithelium of the vestibule is not constant, and often this inconstancy is increased by a widely patulous meatus. This eversion and redundancy of the urethral mucosa is symptomless and does not require treatment

Prolapse of the urethral mucosa may occur. In this condition the urethral mucosa everts itself and projects from the urethral orifice The protruding mass is extremely sensitive and bleeds easily It may be difficult to tell whether the mass is a prolapsed urethral tumor or prolapsed and congested urethral mucosa

Urethrocele or prolapse of the mucous membrane of the urethra has been observed in girls less than 15 years of age. The cause is unknown

Primary tumors of the urethra are rare, but secondary tumors are common. Carcinomas of the bladder, rectum, cervix and anterior vaginal wall may extend to involve the urethra

Benign tumors of the urethra are *urethral caruncles,* in reality polyps of the urethral mucosa. Caruncles are small and are situated near the external meatus They may occur singly or multiply Urethral caruncles are occasionally malignant and therefore biopsy should be performed and they should be treated surgically. Caruncles are symptomless until the mass becomes large The symptoms, when the caruncle is large, are bleeding, pain and dysuria On examination there is a dark red mass protruding from or lying in the urethral meatus Biopsy is diagnostic.

Urethral polyps are not common and are situated in the middle or the posterior portion of the urethra They have the same features as urethral caruncles The diagnosis is made by the endoscopic examination, and when found, the polyps are removed

Malignant tumors of the urethra, *primary carcinomas* and *sarcomas,* like benign urethral tumors, are rare They are distinguished from benign caruncles, polyps, eversion and other lesions by biopsy and microscopic examination

When a mass is found anterior to the vaginal orifice, the correct relationship of the urethral canal to the *mass is ascertained. In a true prolapse the lumen* is directly in the center of the mass Occasionally this condition must be differentiated from urethral polyp, caruncle, condyloma, urethrocele and carcinoma. In urethral polyps the polyp is in the center of the lumen, and the mucosa is around it In caruncle the lesion is usually found only on the posterior lip of the meatus and is very sensitive to touch Condyloma has a warty, fungoid appearance and is usually multiple

The ovaries are frequently found in an unusual position The ovary is recognized by (1) its position, (2) its flattened ellipsoid shape, (3) its movability, (4) its elasticity and (5) its normal characteristic tenderness

In many adults prolapse of the ovary is found, the organ on one or on each side is down in the recto-uterine pouch where it may be either loose or fixed. Often it is very tender.

The vagina and cervix are examined by means of the vaginal speculum. For most purposes, the bivalve speculum is perfectly satisfactory. It is made in several sizes, and the examiner selects that size which can be introduced easily. In children, the most satisfactory speculum is a small cystoscope, which is used in the knee-chest position. In adults, if the hymen is unruptured, one may use a very small bivalve speculum

To introduce the bivalve speculum, one turns it so that its long axis is vertical, to conform to the shape of the vaginal orifice. A lubricant facilitates the introduction of the speculum The common practice of using green soap as a lubricant is not advisable on the first examination, because soap alters the chemical reaction of the vaginal secretions and interferes with staining and cultural reactions. Hence, water or a drop of some jelly on the outer surface of the speculum is a better lubricant

THE VAGINA

The vagina is about 3 inches (7 6 cm) long; its posterior wall is longer than the anterior, being 3½ inches (8 9 cm) long The hollow formed by the anterior wall of the vagina blending with the anterior lip of the cervix is the anterior fornix The depression behind the posterior lip is the posterior fornix, behind which is Douglas' pouch At the vulvar outlet the lumen of the vagina is anteroposterior in direction, it then changes to lateral and at the cervix becomes round Its walls are in contact

Congenital Malformations. Absence of vagina, absence of uterus, double uterus, septate uterus, bicornate uterus, double cervix, and double or septate vagina are anomalies due to *inhibition in the development of the mullerian ducts* The ducts are differentiated and attain a certain degree of development, then, for some reason, normal progress is arrested The result is any one of the aforesaid uterine and vaginal malformations, depending on the point at which fusion is stopped and the amount of maturity which each mullerian duct acquires independently

When there is *nonunion* of the mullerian ducts, the uterus and upper part of the vagina are absent The uterine tubes are separately situated in the lateral parts of the pelvis and each terminates separately and blindly near the midline behind the bladder. These mesial ends often form bulbous enlargements 1 cm. in diameter which are attached to the round ligaments The defect is usually limited to the mullerian ducts, so that ovaries, external genitalia, hymen, vaginal orifice and external segment of the vagina are normal

Women who lack the uterus and vagina menstruate into a uterine tube As the result of successive menstruation into the tubes large pelvic masses are formed

Incomplete union of the mullerian ducts permits of a great variety of uterine and

uterus, and varying grades of duplication may be present One half of the uterus may be normal, the other being a rudimentary horn There may be only one cervix; there may be two. Such defects usually cause no symptoms at all, at times, pregnancy may develop in a rudimentary horn and may lead to serious consequences

The *vaginal defects* due to incomplete union of the mullerian ducts may result in a vertical septum which completely divides the vagina (septate vagina). These septa do not cause serious inconvenience.

Congenital absence or atresia of the vagina may involve the external or the internal part of the vagina.

the uterus, is connected or not connected with the resistance. In addition, dependence is placed on the form and consistency of the uterus as felt by the external hand. The mobility of the uterus (body and cervix) varies according to size and weight of the uterus, the condition of its ligaments, the tension of the abdominal walls, and the state of the adjacent organs. Normally it should be easily possible to press the uterus, with its fundus, upward as far as the upper margin of the symphysis pubis.

The angle between the cervix and the body, when the urinary bladder is empty, is obtuse in normal anteversion and acute in anteflexion. The normal uterus is in a position of antedextroversion, the middle of the fundus gravitating slightly to the right.

On pressing firmly with the two hands near the lateral margins of the uterus, the *broad ligament* (ligamentum latum uteri) on each side may be examined, and abnormal conditions of the parametrium will be found, if present, in the transverse pelvic diameter, to the right and to the left of the uterus.

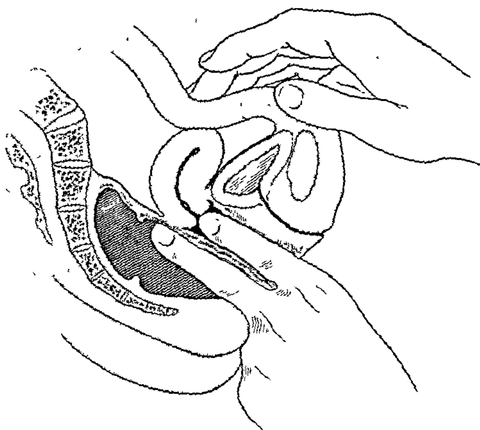


Fig 7-4 Pelvic examination with simultaneous examinations from the rectum and vagina

The *pouch of Douglas* (recto-uterine pouch) behind the uterus and the *peritoneal pocket* between the uterus and the bladder (vesico-uterine pouch) cannot be demonstrated normally on palpation, but if they are filled with blood, ascitic fluid, inflammatory exudate or tumor, the projecting lower part of the pocket can be felt. If doubt about the size or position of the uterus exists after the usual pelvic examination, the examiner may remove some of this doubt by examining the rectum and vagina simultaneously with one finger in the vagina and the other in the rectum (Fig. 7-4).

Dilated and thickened tubes are easily palpable. They are distinguishable from other tissues by their elongated shape which they retain even when enlar d

Leukorrhea is a very common complaint of women. The discharge may arise in any structure from any or no discoverable cause, from Bartholin's glands to the uterine tubes. The commonest causes of leukorrhea for which medical aid is sought are: normal physiologic variations in the amount of the vaginal secretions and unnecessary douching.

A severe vaginal irritation or burn, produced by a douche that was too hot, is followed by leukorrhea. A similar injury may be produced by a douche solution that is too strong or irritating. Infections by pyogenic bacteria, viruses (herpes simplex) and higher plant (yeast) and higher animal (trichomonas) parasites cause vaginal and cervical irritation and leukorrhea.

A yellow fluid discharge is often associated with vaginitis. If bubbles are present, the infection may be due to *Trichomonas vaginalis*. A trichomonad infested vaginal discharge has a foul, sour odor.

Watery, foul-smelling vaginal discharge, often colored, usually contains decomposed blood or organic material. This type of discharge was formerly said to be characteristic of cancer of the cervix, but it is far too common to have such a diagnostic import.

Foreign bodies in the vagina may be the cause of chronic leukorrhea. Objects of many different kinds have been recovered from the vagina, particularly in the insane and in sexual perverts and thieves. Foreign bodies tend to bury themselves in the vaginal wall and may cause considerable pain and discharge. They may slough through into the pelvic cavity, rectum or bladder. They may be so deeply imbedded in the vaginal walls that they can be removed only with the patient under anesthesia. Soda-pop bottles, or similar bottles, should be removed from the vagina by warming the bottle to dislodge the mucous membrane which has been sucked up in the neck of the bottle. Bottles are inserted immediately after removal of the bottle cap in order to use the contents for a contraceptive douche. Bottles become adherent by sucking in the vaginal mucous membrane when the contents of the bottle have been discharged.

Cyclic Changes in the Vaginal Epithelium. In brief, the vaginal mucosa during the lifetime goes through four cycles, each of which coincides with the current degree of ovarian activity. These four cycles are (1) postfetal or newborn, including the first week after birth; (2) infancy and childhood, from the postfetal period to puberty, (3) sexual maturity, puberty to menopause and (4) postmenopausal. The term senile vaginitis describes the postmenopausal change in the vaginal epithelium.

Vaginal Smears. Vaginal smears reflect these cyclic changes and perhaps the cyclic changes wrought by the monthly periods with fair accuracy when viewed by a histologist who is an expert in vaginal cellular morphology.

Tumors of the Vagina. ***Benign Tumors.*** *Inclusion cysts* are from some fragment of vaginal mucosa which is buried under the surface by a perineal laceration or operation. They are often situated on the posterior vaginal wall. Such cysts are difficult to visualize on the anterior wall except when the patient assumes the knee-chest position.

Inclusion cysts are small cysts less than 1 inch (2.5 cm.) in diameter. They are easily identified by the bluish color. As a rule these cysts cause little if any inconvenience.

Endometrial cysts are the result of cystic changes in ectopic endometrium. They are situated in the posterior fornix behind the cervix. These cysts are a part of the general manifestations of endometriosis elsewhere in the ovaries, uterine body or pelvic peritoneum.

Gartnerian cysts are formed by cystic dilatation of the remains (Gartner's duct) of the wolffian ducts. They are 1 or 2 cm. in diameter and are situated on the lateral or anterior walls of the vagina. Small cysts rarely cause symptoms; when large, they

The external type involves only the vaginal orifice, hymen, or terminal part of the vagina. Imperforate hymen is the commonest external vaginal atresia. In this type of lesion the menstrual blood accumulates in the vagina (hematocolpos) or in the uterine cavity (*hematometra*). *The collection of menstrual blood* forms a soft mass which bulges between the labia In these cases the lesion is due to defective development of the mullerian structures. The uterus and uterine tubes are normal

In some instances there may be no external bulging between the labia, but a cystic mass is palpable above the imperforate hymen In such a patient the atresia may involve the lower part of the vagina as well as the hymen

When there is an *internal absence or atresia of the vagina,* there is usually neither cervix nor uterus but the ovaries are present. The external genitalia, vaginal orifice and ovaries may appear normal The vaginal orifice is a shallow depression, rarely more than 1 inch (about 2.5 cm.) deep. It may be of normal width or may be very narrow. *In some instances, owing to efforts at coitus or dilatation, the vagina may be* about 2 inches (5 1 cm) deep

Internal absence or atresia of the vagina is symptomless until the age of menarche or until sexual intercourse is attempted In childhood it may be discovered accidentally by an observant mother or nurse or if accompanied by virilism The persistence of amenorrhea is the first symptom After marriage, the complaint is likely to be inability to have coitus (dyspareunia) or sterility The diagnosis is usually evident on examination.

Agglutination of the labia minord consists in an adhesion of the proximal edges of the labia The appearance of the anomaly is characteristic There is a bluish discoloration near the center of the membrane, formed over the vagina by the labia minora, indicating a space below it. The membrane is thin and is easily depressed by light touch with a blunt instrument

Hermaphroditism. In the human being *true hermaphroditism* is so rare that one should not expect to see it.

False hermaphrodites present the genital glands of one sex in an individual whose secondary sexual characters and external genitalia tend to resemble those of the opposite sex The internal genitalia can be those of either sex. There may be a doubling or mixing but often some of the parts are atrophic. The sex ratio of false hermaphrodites is 3 males to 1 female.

All grades of the *male pseudohermaphrodite* exist The general features are clearly or suggestively masculine, while the external genitalia are clearly or suggestively feminine In these, labial hernias often contain the testicles. After puberty the clitoris becomes large, it may approach the male penis in dimensions. The vagina is usually rudimentary or entirely absent It may open into the urethra. The internal genitalia of the male pseudohermaphrodite are often rudimentary.

In the female pseudohermaphrodite the gonads are ovaries The external genitalia are of either type, although enlargement of the clitoris is not the rule. The general external appearance, voice, bodily contour, distribution of hair, and temperament are usually female The internal genitalia consist of the ovaries, with the accessory male or female organs, when present, in varying degrees of development.

Hermaphrodites may be reared and trained as members of the sex opposite from their gonads During childhood this is serious; with the onset of puberty it is often tragic

Leukorrhea. The vaginal mucous membrane is protected by variable amounts [illegible] Excessive but normal increase of [illegible] near menstrual periods, at [illegible] he result of fatigue, excite- [illegible]

Childbirth injures the cervical tissues A lacerated cervix may become infected and never heal completely. A failure to heal of an obstetric injury, an infection or a surgical operation may cause stenosis of the cervix resulting in painful menstruation and sterility.

There may be no symptoms of chronic cervicitis. Often, however, there is leukorrhea. Rarely does chronic cervicitis give general symptoms

On examination there are areas of redness, eversion of the mucosa, scars, redundant granulations, and dilated glands—all of which are indications of cervical injury and infection

Chronic cervicitis which has followed an unhealed scar may have sharply defined borders or be diffuse to the reflection of the vagina, presenting the appearance of a chronic irritation There may be present yellowish or bluish cystic cervical glands. Some cervices are completely distorted by deep scars; they may be swollen,

Granulomatous Lesions of the Cervix. *Tuberculosis.* Incidences of tuberculosis as reported vary considerably. Counsellor and Collins recorded that the patients were 20 to 40 years of age in 73 per cent of their cases and stated that marriage and pregnancy are contributing factors in the disease

Tuberculosis of the cervix is primary if other foci are absent. The origin of primary cervical infections is by introduction from the outside This means of infection is exceedingly rare The lesions are secondary to foci in the lungs, the upper part of the genital tract, and the gastrointestinal tract

Different types of lesions occur The ulcerative type is most commonly seen and appears as a large region of deep ulceration with ragged undermined edges and a red, soft, easily bleeding, granulomatous base Ulcerative and papillary lesions may occur which are not grossly distinguishable from carcinoma.

The bleeding may be spotty or profuse. Often there is postcoital spotting. Leukorrhea is also a prominent symptom, the discharge is grayish yellow, thick, profuse and foul because of the destruction of tissue and the presence of caseous material Loss of weight, night sweats, anemia and weakness may be present, but generally these are due to the presence of tuberculosis elsewhere in the body. Pelvic pain is present with secondary infection or with tuberculous extension to the vagina, parametrium and upper part of the genital tract.

Clinically the diagnosis is seldom made unless *Mycobacterium tuberculosis* is found in the vagina or in the injected guinea pig The *Mycobacterium tuberculosis* cannot be differentiated from the *Smegma bacillus* in stained preparations.

Granuloma Inguinale. The cervix is one of the primary or secondary sites of granuloma inguinale

The specific etiologic agent is a microorganism which characteristically forms Donovan bodies (Donovania granulomatis), it has not been cultured and is pathogenic only for man The symptoms do not vary from those of carcinoma, but the youth of the patient is suggestive of a nonmalignant lesion.

On examination the early lesion appears as a shallow ulcerated area with well-defined edges and a diffuse, red, granulomatous base The advanced lesion consists of a large fungiform excrescence of soft, red, friable tissue replacing part or all of the cervix

The diagnosis depends on a demonstration of the Donovan body in smears, scrapings or a biopsy specimen Better results are obtained by the use of biopsy than from smears or scrapings Diagnosis is by no means a simple matter in chronic instances, since the characteristic monocytes may be scarce.

may interfere with sexual intercourse or with labor. The commonest complaint is the foul odor from the interference with normal discharge and drainage of urine

A large vaginal cyst in the anterior fornix may simulate a cystocele. A cystocele is emptied by urethral catheterization, whereas a cyst is not.

Papillomas and *polyps* are small sessile or pedunculated excrescences, often multiple, and are situated anywhere in the vagina.

Condylomas are polypoid growths that are of inflammatory origin Often they are due to syphilis, gonorrhea or other infection. Pregnancy and obesity favor the development of vaginal polyps and condylomas

Fibromas and *myomas* of the vaginal walls are rare. They may occupy any part of the vagina, and they occasionally attain large size. They are firm, movable tumors with a smooth surface

Granulation tissue may occur in vaginal scars Granulation tissue may arise in the margin of the vaginal scar after total hysterectomy These may be carcinomas if the patient has been operated on for carcinoma of the body of the uterus.

Malignant Tumors. The *carcinomas* of the vagina are commonly of secondary origin They occur in women past the menopause or older

Primary carcinomas may occupy any part of the vagina They are highly malignant, ulcerated, friable and indurated tumors which are fixed to the subjacent tissues. They invade the rectovaginal or vesicovaginal septum or urethra with the formation of fistula, urinary incontinence, infection, pain and incapacitation. They metastasize to the inguinal and pelvic lymph nodes. The earliest symptom is vaginal bleeding or discharge. On examination an indurated, fixed ulcerating lesion of the *vagina of an elderly woman is usually a carcinoma. Biopsy is diagnostic*

Secondary carcinomas of the vagina originate from carcinoma of the uterine cervix and uterus Anal and rectal carcinomas often extend to involve the vagina

Sarcomas of the vagina are rare They may be present in infants and in children, although no age group is entirely immune Vaginal sarcomas differ from benign polyps in being much harder, fixed to the deeper tissues, and invasive.

THE UTERINE CERVIX

The uterine cervix is the rounded knoblike end of the uterus which opens into the vagina It varies greatly in size and length in nulliparae It is about 1 inch (1 to 3 cm) in diameter. Occasionally it extends into the vagina as a cone-shaped projection 1⅕ to 1⅗ inches (3 to 4 cm) in length. The cervical canal opens into *the vagina by the external os and into the uterus by the internal os* The external os in nulliparae is round, but in those who have borne children or in those who have had deep cauterization it is an irregular transverse slit. The cervical canal is narrowed at both the internal os and the external os and is larger between, hence when instruments are passed into the uterus, they traverse with difficulty the external os and the internal os but pass readily between the two and into the uterine *cavity beyond*

The shape of the cervix and of the external os is so variable after childbirth that descriptions are impossible. Mutilations of the cervix worse than those of childbirth are rendered to it by surgeons in deeply cauterizing it or attempting to amputate it.

Chronic Cervical Irritation (Cervicitis) Many different kinds of organisms cause chronic infection of the cervix Of the bacteria those commonly present in chronic infections are the gonococcus, tubercle bacillus and various other pyogenic infectious agents. The cervix may be injured by fungi and *Trichomonas vaginalis*.

The glands of the cervix may become infected and if so they are often occluded An occluded infection in the cervix frequently becomes enclosed and chronic and persists.

grades of malignancy and for this reason length of survival usually but not always coincides with the grade of malignancy revealed by microscopic study.

There are no early or first *symptoms* of carcinoma of the cervix. There may be irregular bleeding and vaginal discharge In the life of a woman irregular bleeding and vaginal discharges are so common that she is forced to accept these as temporary inconveniences. Assuming that all agreed that in an attempt to detect all carcinomas of the cervix early enough for cure, biopsy be performed on every woman who has a vaginal discharge and irregular bleeding, it would soon be realized that these symptoms are not always present with carcinoma, for many women who have carcinoma of the cervix do not have bleeding until the late stages of the disease Some women who have died of carcinoma of the cervix were examined early by those skilled in the art of examination, and it was not until symptoms of widespread malignant disease were present that a diagnosis was made. This will continue to happen, despite all that can be done, until more is learned about this disease. It is impossible to estimate the stage of invasion by the duration or amount of bleeding Bleeding may occur only after coitus. Leukorrhea may come on early in the disease, it has no particular diagnostic significance even if the discharge is blood tinged Bloody leukorrhea is more significant of a benign polyp than of carcinoma. Pain in the course of cervical malignant disease is an unfavorable symptom, since it often indicates an extensive growth

On *examination* the earliest carcinoma of the cervix is superficial, limited to the epithelium or may be present in situ and thus it does not invade the subjacent tissue. In this stage the lesion cannot be identified by its gross appearance In the early carcinoma of the cervix, the malignant change may extend over the cervix or may remain localized near the cervical os For these reasons early carcinomas are discovered only during the microscopic examination of material removed for biopsy.

As the growth becomes invasive, the appearance of the cervix on examination may reveal that the tumor has grown externally, producing an ulcerating mass on the cervix In contrast to this the growth may have extended into the depth of the cervix leaving minimal surface changes However, as the tumor develops, it extends to the surrounding structures The degree of involvement of the extracervical tissues is important both diagnostically and therapeutically.

On palpation there often is extension into the broad ligament and the bladder, and posterior extension along the uterosacral ligaments to the sacrum, the rectum and the sacral nerve roots The regional lymph nodes are involved in the following order of frequency, hypogastric, obturator, ureteral and external iliac Lymph-node involvement is always indicative of extensive malignant disease

The foregoing findings on examination are clearly identified in the *Annual Report on the Results of Radiotherapy in Carcinoma of the Uterine Cervix* (1952) (the so-called *League of Nations' Classification*) The 12 representatives meeting in session on the occasion of the International and Fourth American Congress of Obstetrics and Gynecology in May, 1950, agreed that the staging of carcinoma of the cervix should read as follows (quoted by permission of the Editorial Committee)

Stage O Carcinoma in situ—also known as pre-invasive carcinoma, intra-epithelial carcinoma—and similar conditions

Stage I The carcinoma is strictly confined to the cervix

Stage II The carcinoma extends beyond the cervix but has not reached the pelvic wall The carcinoma involves the vagina but not the lower third

Stage III The carcinoma has reached the pelvic wall. (On rectal examination no "cancer-free" space is found between the tumour and the pelvic wall.) The carcinoma involves the lower third of the vagina.

Stage IV The carcinoma involves the bladder or the rectum, or both, or has extended beyond the limits previously described.

Syphilis. A chancre of the cervix in the stage of recognizable development appears as a deep, funnel-shaped sore with thickened, rounded edges which slope down to a smooth base

The macules of secondary syphilis of the uterine cervix appear as grayish-white, slightly elevated areas. Large macules or confluences of smaller ones are termed mucous patches. The erosion of the mucous patch is covered with a pinkish or a grayish exudate which may contain spirochetes. Secondary syphilitic ulcers are associated with yellow, mucopurulent vaginal discharge.

The gumma undergoes ulceration and necrosis; or occasionally, tissue prolifera-tion occurs so that a fungating, soft mass replaces most or all of the cervix.

The diagnosis of primary and secondary lesions depends on the finding of *Treponema pallidum* by darkfield examination, since results of serologic tests are not always positive until three weeks after the initial infection. The tertiary lesion (gumma) is diagnosed by biopsy and positive serologic tests.

Chancroid. Chancroid of the cervix is rare Symptoms include soreness in the lower part of the abdomen, grayish vaginal discharge and burning and pain in the vagina. On examination there may or may not be ulcers of the external genitalia and inguinal lymphadenopathy. Pronounced vaginal tenderness is present The cervix appears to be red and edematous with one or more round, firm, punched-out, ulcerated lesions on the portio vaginalis. The ulceration may be covered with an easily removable whitish exudate. Diagnosis is established by smear, culture, skin test and biopsy (see p. 410).

Tumors of the Cervix. Benign Tumors. *Cervical polyps* usually occur in adult women, rarely before the age of 30 years For practical purposes cervical polyps are not malignant, but malignant changes occur frequently enough to require histologic examination of every polyp that is removed.

Cervical polyps are among the commonest causes of intermenstrual bleeding They may cause leukorrhea and may produce sterility Some cervical polyps, if large, can be felt on palpation On visualization a cervical polyp appears more reddened and of a deeper color than the cervix. It usually projects from the cervical os and can be moved about by means of a cotton swab. These polyps often bleed easily when traumatized .They are differentiated from prolapse of the mucous membrane of the cervix by their mobility and microscopic structure.

Since most myomas develop in the body of the uterus, *cervical myomas* are rare and they seldom are diagnosed prior to operation.

Malignant Tumors. *Carcinomas* of the uterine cervix usually occur in women who have borne children and who are between the ages of 40 and 55 years They develop in the regions of chronic irritation, epithelial erosion, unhealed laceration and in polyps.

Macklin studied the morbid heredity in cervical cancer, and her conclusions leave little doubt that in certain families, but only in certain families, does heredity seem to play a part in the incidence of carcinoma Jewish women rarely, if ever, have malignant cervical polyps and cervical carcinoma

Carcinoma of the external cervix of the uterus arises from the vaginal portion including the transition zone at the external os Carcinoma of the endocervix arises between the internal os and the external os of the cervix

Carcinoma of the cervix has offered difficulties in classification. Cervical carcinomas are chiefly of the squamous cell variety A few adenocarcinomas are encountered Either the squamous cell carcinoma or the adenocarcinoma can be classified on the basis of anaplasia. Broders' classification is based on anaplasia In this grouping grade 1 [illegible] malignant, show the greatest tendency [illegible] and grade 3 carcinomas show greater [illegible]ile those of grade 4 are the most ana-[illegible]nt It is recognized that most cervical carcinomas are mixed tumors, [illegible]ly contain cells of various types and

The *diagnosis* is established by biopsy. If the cervix is chronically irritated or ulcerated in middle-aged women, and in some young women, even if there are no symptoms, cancer is suspected

Meigs and Jaffe found in their analysis of the survival rates of patients undergoing irradiation that most of the deaths occur in the first 2 years and that most patients without obvious disease at the end of 2 years have a good chance for recovery. Kimbrough and Tompkins found that 23 3 per cent of the patients survived 5 or more years and that 18.7 per cent of the original group lived more than 10 years after treatment

Bleeding from the cervical stump is a serious symptom, for it is most frequently due to carcinoma If cervical carcinoma appears within a year after hysterectomy, it was probably present at the time of the operation Biopsy is diagnostic.

Many have expressed the belief that carcinoma of the cervix in *pregnant women* progresses more rapidly than in older nonpregnant women. It should be realized that a cervical carcinoma tends to cause abortion. The presence of carcinoma generally is an indication for abortion The religious beliefs of the patient should be respected after the stark facts have been presented to her.

THE UTERUS

Attachments of the Uterus In addition to being attached to the vagina, the uterus has certain folds or ligaments which pass from it to the surrounding parts Anteriorly the peritoneum is reflected from the uterus at the level of the internal os to the bladder, forming the *uterovesical fold*. Posteriorly the peritoneum descends from the uterus over the posterior surface of the upper portion of the vagina for about ½ inch (1 3 cm) and thence onto the rectum, constituting the *rectovaginal* or *recto-uterine fold*. The deep pouch so formed is called *Douglas' pouch* On each side are three ligaments, of which the *broad ligament* is the largest and most important The two broad ligaments and the uterus form a diaphragm which extends from one side of the pelvis directly across to the other, thus dividing it into anterior and posterior compartments

At its pelvic attachment the broad ligament widens out, having the round ligament as its anterior edge and the *infundibulopelvic* or *suspensory ligament* of the ovary as its posterior edge Immediately posteriorly is the *uterosacral ligament* (recto-uterine), it runs from the uterus backward and contains muscular and fibrous tissue, the muscular tissue goes to the rectal wall, while the fibrous goes to be attached to the second and third sacral vertebrae This ligament on each side forms the outer border of Douglas' pouch These ligaments may become sensitive if the so-called *uterosacral syndrome* ensues

The round ligament leaves the cornu of the uterus just below and anterior to the uterine tube, and passes outward, forward, and slightly upward to reach the internal inguinal ring and canal, through which it passes to end in the subcutaneous tissue and skin of the labium majus pudendi.

Congenital Malformations. See malformations of the vagina, page 449.

Chronic Subinvolution. Chronic subinvolution of the uterus occurs after childbirth, most frequently in women between 35 and 45 years of age However, the condition may appear in any woman who has had a baby

The pregnant uterus contains an increased amount of elastic tissue in its walls and in the enlarged blood vessels In the course of normal puerperal involution of the uterus the increased amount of elastic tissue in the myometrium and vessel walls is absorbed and new vessels of smaller caliber are formed When this elastic tissue is not properly absorbed, degenerative changes follow. The connective tissues undergo liquefaction and hyalinization and become edematous because of failure of re-establishment of an efficient circulation The uterus remains enlarged

The common symptoms are profuse menstruation, intermenstrual bleeding, leukorrhea and pelvic pain. On examination the uterine body is diffusely and symmetrically enlarged An exact diagnosis is made only by microscopic study of the excised uterus

This classification was adopted by the three American societies and recommended by the Subcommittee of the World Health Organization on the Registration of Cases of Cancer and their Statistical Presentation.

In stage-grouping the following general rules should be observed:

When allocating a case to a stage nothing but facts revealed by examination should be taken in account.

The stage of each case should be decided at examination prior to treatment and this classification should remain. The classification may be postponed quite exceptionally and the reasons stated.

When it is doubtful to which stage a given case is to be allocated, the earlier stage should be chosen

The fact that a single case presents two or more of the conditions which characterize a particular stage does not affect the staging.

The Editorial Committee recognizes that the classification of 1950 represents a large step forward but considers that in regard to the uniform presentation of statistics on carcinoma of the cervix, there are a few points which need further explanation.

1 The type of case to be allocated to Stage O should be strictly defined. This must be deferred until further experience on the subject has been accumulated Pending such definitions the collaborators are earnestly requested to allocate to Stage I only such cases in which the presence of an invasive carcinoma is beyond doubt

2. The signs which characterize involvement of the bladder should be defined Cases in which on cystoscopy there is no fistula, no ulcerating tumour and no tuberculi visible but which show bullous oedema or ridges and furrows are difficult to classify

The Editorial Committee suggests that.

(a) A bullous oedema should only be considered as a sign of involvement of the bladder if the diagnosis is microscopically verified, (b) Ridges and furrows should only be interpreted as a sign of involvement of the bladder if they remain during palposcopy This method of examination implies coincident cystoscopy and digital examination of the bladder trigone by rectal palpation Where there is no carcinomatous involvement of the bladder wall the ridges and furrows will disappear when the trigone is lifted up The method has not previously been described It has been used for many years at the Radiumhemmet, Stockholm, as a routine examination in all cases of cervical carcinoma

3 According to the classification of 1950, a case should be allotted to Stage II if the involvement of the parametrium "has not reached the pelvic wall," and to Stage III if it "has reached the pelvic wall" The definitions of 1937 state "has not invaded the pelvic wall" and "has invaded the pelvic wall" The Editorial Committee is of the opinion that it should be seriously considered at a future revision of the definitions which of these two versions is more suitable

The study of *vaginal smears* as a means of early diagnosis of cervical or uterine cancer was advocated and practiced by Papanicolaou Cervical cancer is revealed in vaginal smears by the appearance of characteristic cells derived from the superficial layers of the tumor, which undergo continual desquamation These cells show great variety of form and size, much greater than that seen in sections of the tumor. The most characteristic feature of the abnormal cells is the atypical form and structure of their nuclei and vacuolization of the cytoplasm A commonly found, characteristic cell type is an extremely elongated one resembling a smooth muscle fiber. Erythrocytes are generally found in large numbers. Block warned, however, that a positive diagnosis from a vaginal smear does not indicate immediate radical intervention or irradiation but rather that confirmatory biopsies of the cervix or endometrium should be performed.

The commonest cause of spontaneous abortion is the intrinsic factor comprising malformations of the fertilized ovum.

There are two groups of *extrinsic* factors which may precipitate spontaneous abortions. These are the environmental factors external to the body and the factor of disease within the body. For instance, it is said that women during the first two or three months of gestation should avoid excesses of drugs, alcohol, cold, heat, trauma, exertion, infections and local stimulation.

The diseases within the body which are potent in the production of spontaneous abortion are pyogenic infections, gonorrhea and tuberculosis. Tumors such as myomas and ovarian tumors may cause abortion. Uterine retroflexion, laceration and injury to the cervix, repeated pregnancies, uterine hyperirritability, congenital malformations and constitutional diseases all may precipitate spontaneous abortion Diabetes may be associated with abortion. If a woman who has an endocrinopathy should conceive, the pregnancy is likely to terminate in spontaneous abortion.

A general anesthetic drug, quinine and castor oil, turpentine, ergot, irradiation and trauma may cause spontaneous abortion All sorts of herbs, and folk medicine consisting of pastes and solutions, are used for intra-uterine injection to produce spontaneous abortion or to bring on the period.

In regard to physical exercise, it is observed that a healthy ovum in the uterus of a hardworking woman is not dislodged by any sort of ordinary, or even laborious, task performed by her. A diagnostician is loath to attribute abortion to many of the overemphasized inconsequential causes.

On the basis of the relative completion of the process, abortions are termed threatened, inevitable, complete, incomplete and missed. The symptoms, diagnostic findings and therapy vary with the type that is present.

In a *threatened abortion* the bleeding is slight and the pain, if any, is only moderate It is a discomfort in the lower part of the abdomen. The cervix is not dilated

In *inevitable abortion* the cervix is dilated, membranes are often ruptured, and bleeding is profuse or has persisted despite rest The uterine contractions return as soon as opiates and rest are discontinued In such cases the process is hastened to completion.

In *incomplete abortion* the uterus has been partially emptied spontaneously or intentionally If there are no manifestations of infection, it is best to complete the abortion All abortions should be considered to be infected

Habitual abortion has possible endocrine, gynecologic and urologic associations. However, in many instances no disturbances to account for an abortion can be demonstrated in any of these categories

In a *missed abortion* the membranes and the fetus are still in place. The fetus is dead There is amenorrhea, followed by slight bleeding, with some pelvic discomfort. The uterus does not increase in size as the pregnancy lengthens Soon toxic or absorptive phenomena, malaise, headache, nervousness and apprehension supervene. The absence of a positive reaction to Friedman and Aschheim-Zondek tests or one of these tests for pregnancy would confirm the diagnosis

Therapeutic (Induced) Abortion. A therapeutic abortion is performed as a part of the treatment for some disorder that concerns the mother or the fetus. The indications for a therapeutic abortion vary so widely that only one rule can be given for the diagnostician to follow This rule is never to advise a therapeutic abortion on data supplied by anyone else. Weigh all the findings obtained as the result of personally conducted examinations and from these data make a decision. It is well to remember that a therapeutic abortion may carry some risk to the patient, depending on her physical condition.

Rape resulting in pregnancy is an indication for abortion (see p 479).

Hypertrophy. There are women who have diffuse enlargement of the uterus as the result of hypertrophy of the muscle. In view of the presence of endometrial hyperplasia in all of these cases, it is suggested that the uterine enlargement may be in a measure due to hyperestrogenism

The symptoms are menorrhagia, metrorrhagia, leukorrhea and pelvic pain On examination the uterus is diffusely enlarged. Microscopic study of the uterus establishes the diagnosis.

Primary Dysmenorrhea. Dysmenorrhea is present in approximately one third of menstruating women. It commences with the menarche. The distress starts the day prior to or with the menstrual flow and consists of cramps in the lower part of the abdomen which may or may not be associated with backache, headache, nausea and vomiting It persists through the first or second days of the flow. There may be prodromal irritability, backache, headache and gastrointestinal upsets The dysmenorrhea may partially or wholly cease after the birth of the first child. After the age of 30 years in the nulliparous woman the dysmenorrhea may become irregular and of lessened intensity.

It is agreed that there is no consistent anatomic lesion in patients who suffer from primary dysmenorrhea It is not due directly or indirectly to a retroverted, anteflexed or infantile uterus, cystic ovaries, presacral neuritis, defective uterine musculature or disturbed innervation

The pain experienced is due to uterine contractions. This point of view is confirmed by the experimental work of Moir and Bickers, working separately, and of Randall and Odell. Ovulation is a necessary precursor to painful menses. The presence of secretory endometrium (suction biopsy) as recorded by Randall and Odell and Sturgis and Albright renders this premise certain. Ovulation is prevented by diethylstilbestrol and thus there is no development of secretory endometrium, and painless menstruation ensues.

The presence of backache, nausea, vomiting and headache can hardly be explained on an organic basis. Premenstrual tension, as evidenced by abdominal pain, irritability, headache, backache and nervousness, is on a psychogenic basis. These patients should be assured that they are absolutely normal and should receive an explanation in simple terms of the basic physiology of menstrual distress Some relief of pain can be obtained with simple analgesics, particularly after the patient realizes the nature of her complaint

Infections of the Uterus. Infections of the endometrium are usually a part of a diffuse genital infection. Endometritis following childbirth is a serious condition which may leave permanent sequelae Tuberculosis, trauma, foreign bodies and tumors may cause endometritis

In the acute stages of puerperal sepsis the uterine wall may be severely infected and if uterine drainage is poor, a chronic metritis may persist indefinitely.

Chronic Metritis. *The condition occurs in both parous and nulliparous women.* Often there is an associated inflammatory lesion in the uterine tubes Occasionally chronic endometritis without obvious lesions of the appendages may be encountered. Chronic subinvolution and chronic metritis may occur in the same uterus. In this event there are the pathologic changes that mark both these conditions The symptoms are menorrhagia, metrorrhagia, leukorrhea and pelvic pain. Examination reveals an enlarged uterus Diagnosis is made by microscopic examination of the uterus.

Abortion. For diagnostic purposes all abortions are either spontaneous or induced

[illegible] may [illegible] *rinsic*

factors

the uterus is enlarged and usually smooth in outline. If menstrual bleeding has been excessive, there is anemia.

The diagnosis is made by biopsy of uterine tissue. The history and the examination may in some instances be almost conclusive. In others, not even a suggestion of the true condition will be evident. Myoma, chronic subinvolution of the uterus, and adenocarcinoma of the endometrium are differentiated by endometrial biopsy.

External Endometriosis. By definition, in external endometriosis the endometrium has been transplanted or has originated outside of the uterus (Fig 7-5). An internal endometriosis also may be present and vice versa

The theories of the origin of external endometriosis are (1) embryonic rests, (2) metaplasia and (3) transportation of either uterine or tubal epithelium

The theory of embryonic rests of cells derives its plausibility from the fact that epithelium of the uterine tubes and uterus and the germinal epithelium of the ovary all have a common origin in the celomic epithelium In the ultimate distribution and differentiation of the celomic epithelium it is postulated that it may be scattered from the umbilicus to the knees

As the result of irritation, inflammation or hormonal disturbances the pelvic peritoneum undergoes metaplasia, changing into columnar epithelium and forming glands that resemble endometrium or tubal mucosa in appearance and function.

Adult epithelium, tubal or uterine, may be transported to the ectopic sites by the lymphatics, veins and peritoneum, or by surgical operation. As the lesions progress, rupturing of the cysts gives rise to implants throughout the pelvis. The fluid from an endometrial cyst is irritating and produces peritoneal reaction with subsequent adhesions cementing the pelvic viscera together. The lesions of endometriosis are black or brown, puckered or cystic areas. The lesions are often situated on the undersurface of the ovary and the adjacent part of the broad ligament, and on the posterior surface of the cervix along the attachment of the uterosacral ligaments.

Endometrial tissue in or near the umbilicus of the abdominal wall appears as bluish cysts which swell and which may discharge blood with each menstrual period When the lesion is found in an abdominal scar, there is a history of some uterine or tubal operation

There have accumulated reports of many instances of endometrial tissue being present in the sigmoid colon Many of the patients who have these sigmoid lesions have suggestive histories and findings of endometriosis only in retrospect after the diagnosis is established by biopsy.

The presence of endometrial tissue in the bladder causes frequent and painful micturition

After the menopause, whether induced by surgical intervention, irradiation or nature, endometrial tumors retrogress

Many women who have endometriosis have no symptoms referable to the pelvic [illegible]

[illegible] significant.

On examination, if the external lesion, like a vaginal or umbilical cyst, can be seen, it is almost diagnostic in appearance, but lesions of this type are rare. When cysts are brought into view by means of the vaginal speculum, artificial light can be caused to reflect and they shine as do the eyes of an animal at night.

On palpation the significant findings are in the adnexa. About the cervix and in the rectovaginal septum hard nodular, rather fixed lesions are often palpable The ovaries are fixed and enlarged and vary in tenderness The uterus is often retroflexed, and in women more than 35 years old is often myomatous

A definite diagnosis is established by biopsy. However, in a young woman

Endometriosis (Adenomyoma, Adenomyosis and Endometrioma). When uterine or tubal mucosa is situated anywhere except in its normal position in the tubes and the uterus, the condition is termed endometriosis. Endometriosis may be internal (uterine) or external (extra-uterine)

The usual and unusual distributions of the lesions are shown in Figure 7-5. The lesions often are multiple, occurring in more than one organ. The incidence of endometriosis is not known but the disease is common.

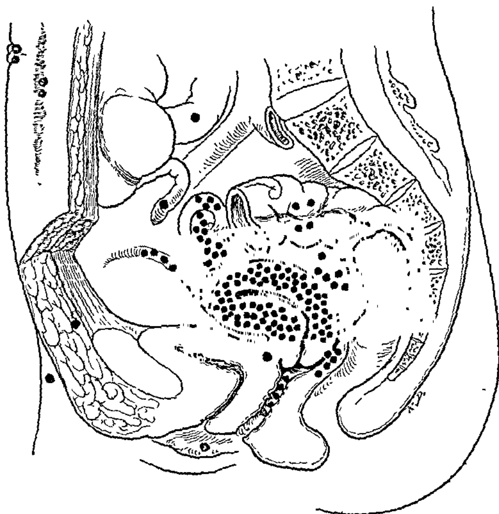


Fig 7-5 Endometriosis The commonest sites of occurrence are indicated.

Internal Endometriosis. When endometrium is found disseminated throughout the uterine wall, the condition is termed internal endometriosis In internal endometriosis the epithelial tissue is continuous with the endometrium which lines the uterine cavity.

The ectopic endometrium is scattered throughout a part or all of the uterine wall When the epithelial elements are collected into nodules, the condition is termed endometrioma When these epithelial elements are in muscle tissue they are termed adenomyoma.

The first symptom of uterine endometri... d of infertility followed by symptoms of pressure of th... rual irregularities The menstr... and menorrhagia The ... by intense pain On pelvic examination

advanced pregnancy is detected by the presence of fetal movements and fetal heart sounds, and by roentgenologic evidence

Endometrial cysts, chocolate cysts and tubo-ovarian masses simulate uterine myoma and are often associated with fibroid tumors of the uterus. Small asymptomatic myomas do not require treatment. Large tumors should be removed

Malignant Tumors. *Carcinoma of the endometrium* occurs more frequently in women after the menopause than in younger women. The first symptom is frequently postmenopausal bleeding If the tumor occurs prior to the menopause, intermenstrual bleeding and profuse menstruation occur In the beginning the bleeding is slight and transitory and may never be more than an intermittent brownish or bloody tinge in leukorrhea which has been present for a long time Leukorrhea is not significant. As the growth advances, however, the discharge may become more profuse and foul. On examination the uterus is somewhat enlarged and soft The diagnosis is made by microscopic examination of the endometrium.

Papanicolaou became aware that carcinoma of the fundus of the uterus as well as carcinoma of the cervix (see p. 456) are to some extent exfoliative lesions in the sense that cells at the free surface of the growth tend to become dislodged and subsequently to find their way into the vagina He developed a method for collecting the cellular debris from the uterus as well as the cervix, which is smeared on glass slides and stained in a particular way so that the various components may be studied The method is simple and may be applied to large numbers of women Papanicolaou states that cells pathognomonic of cervical and fundal carcinoma can be definitely recognized. The interpretation of smears calls for an intimate knowledge of the cytologic characteristics of the vaginal fluid

Malignant cells will not always be present in every smear from cases of cancer even though the tumor may be very large and clinically obvious The method seems to be used as an adjunct rather than a substitute for biopsy and histologic examination

Primary sarcoma of the uterus is very rare When present, it occurs in the walls of the uterus

Secondary sarcoma in a myoma is rare The frequency of sarcomatous changes in myomas is not known

When sarcoma is present in a myoma, there is rapid growth, and often pain. These rapidly growing myomas may occur after the menopause, when myomas should decrease in size The examination reveals a tumor that feels like a myoma

The diagnosis is not made until the tumor is examined histologically.

Tumors of the Chorion. Benign Tumors. A *hydatid mole* (hydatidiform mole, vesicular mole) is a rare lesion When it occurs, it follows pregnancy by several months to 2 or 3 years

The hydatid mole may invade the entire thickness of the uterus and perforate the peritoneum. This may produce peritonitis and intraperitoneal hemorrhage.

Embolic transplantation of fragments of hydatid mole tissue has been observed in the vaginal walls, the parametrium and the lungs Transplantation of this tissue does not indicate metastasis, as is observed in malignant disease A certain percentage of benign hydatid moles, however, become malignant chorionepitheliomas.

Intermittent uterine bleeding is a symptom There are periods of active bleeding, between which a serosanguineous discharge appears Soon there are pain in the lower part of the abdomen, weakness, and often anemia. Abortion is frequent The abortion is accompanied by hemorrhage which is usually profuse, prolonged and sometimes fatal because uterine muscle may be invaded and unable to contract vigorously.

On examination the uterus seems to be pregnant, although there are no evidence of the fetus, no fetal heart beats, no fetal movements, and no fetal shadow on roentgenographic examination Reactions to the Friedman and the Aschheim-

who gives no history of a pelvic infection and who has hard nodular lesions about the cervix and retrovaginal tissues with fixation of the ovaries in association with sterility and progressive dysmenorrhea, the diagnosis is reasonably certain to be endometriosis.

In the differential diagnosis consideration is given to (1) chronic salpingitis, (2) uterine myomas, (3) the presence of ureteral renal and ureteral stones and (4) lesions of the pelvic colon.

Endometriosis of the rectovaginal septum is distinguished from carcinoma by the presence of endometriosis elsewhere, the absence of metastasis and presence of endometrial cysts behind the cervix.

Uterine Neoplasms. ***Benign Tumors.*** The myomas, the fibromas or the myofibromas comprise the major part of the important benign tumors of the uterus.

A *uterine myoma* is a benign tumor composed of smooth muscle and connective tissue. This type of tumor is known also as fibromyoma, myofibroma, leiomyoma and fibroma The etiology is unknown.

Myomas are common in women of all races. They are most frequently found in women from 40 to 45 years of age, although they may occur in young women; the age limits are usually given as from 30 to 55 years Uterine myomas have a wide range of size, situation and shape.

Myomas are often referred to according to their situation; for instance as intramural, subperitoneal or submucous The large myomas show hyaline and cystic changes Suppuration and formation of abscess are rare Incomplete or complete calcification may occur. Intramural myomas may cause intramenstrual bleeding

Generally uterine myomas are symptomless. Symptoms do occur, however, and when present are due to changes within the myomas, to degenerations, to unfavorable anatomic relationships and to submucous development The common symptoms are pain, tumor, menorrhagia and sterility The patient may first palpate the mass, which may reach the umbilicus before there are symptoms. More frequently, however, a large myoma is sensitive to pressure There is pain which is due to a complicating adnexal or pelvic disease The pain may be a sensation of pressure, or dysmenorrhea, dysuria, painful defecation or a sacral backache Occasionally it is referred down the thighs or up into the ureteral or the renal regions

Dysmenorrhea is often associated with profuse menstrual bleeding.

On routine pelvic examination of women who have attained the late thirties or more, a few of them, by no means all, will have one or more myomas. The myomas are an insensitive uterine enlargement which is nodular, hard and movable The masses are usually round and multiple and vary in size up to those which occupy the entire abdomen. A large myoma which has undergone degeneration may be soft and cystic and cannot be distinguished on palpation from a normally pregnant uterus or an ovarian cyst Small myomas which are clustered about the uterus cannot be differentiated by physical means from an endometriosis

Anemia may result from the menorrhagia and may be serious Occasionally anemia is encountered in women who have myomas but who have not had bleeding These anemias are the same as those present in many women who menstruate These anemias can be corrected by the administration of iron, or the patients may spontaneously recover after hysterectomy

In diagnosis a tumor situated in or adherent to the uterus without symptoms is usually a myoma, and such a tumor associated with the forementioned symptoms is nearly always a myoma.

A soft myoma, causing symmetric enlargement of the uterus, is indistinguishable on palpation from a normal pregnant uterus The Aschheim-Zondek, Friedman and frog tests are the most certain methods of detecting an early pregnancy. A more

LOCALIZATION. The vaginal epithelium in children, in women during pregnancy, and in senile women is thin, its secretions are but slightly acid, and it offers slight resistance to the gonococci

The vaginal epithelium of the adult nonpregnant woman is thicker, produces a stronger acid secretion and is resistant to gonococci In young women gonorrheal vaginitis is usually slight and transient and there is no localization in the vagina and cervix as is observed in girls and in aged or pregnant women. Gonorrheal endometritis is generally transitory

In the periurethral ducts of Skene and the vulvovaginal and cervical glands the gonococcus grows and produces its full effects There are swelling and inflammation which occlude the openings to the ducts and result in acute, chronic, deep and permanent infections, and formation of abscesses and cicatrices. If the tubal openings are closed by the inflammation, pyosalpinx and hydrosalpinx are often present. Sterility, recurring exacerbations of the infection, pelvic peritonitis and pelvic abscess are serious complications resulting from gonorrheal salpingitis. If the tubes remain open, as they usually do, no serious sequelae are observed. As a rule, a localized pelvic peritonitis accompanies salpingitis

Ophthalmia, when it ocurs, is usually a direct contamination transmitted from the genital tract to the eyes by the hands.

Among metastatic infections (lymphogenous or hematogenous) are adenitis, septicemia, endocarditis, hepatitis, arthritis, periostitis, osteomyelitis, tenosynovitis and dermatitis All of these are described under their respective headings elsewhere in this text.

The chronic foci of infections in the external genitalia are the cervical glands and epithelium, Bartholin's glands and Skene's glands In children and in the aged or the pregnant woman the vagina is the focus of chronic infection

The infection becomes chronic by closing or constricting the ducts of the glands. This interferes with the escape of infectious material for long periods of time The material which collects thus may form an abscess. In time, if the abscess resolves, the fluid in the occluded gland may be clear or translucent, the gland being changed into a cyst This cyst in turn may become an acute pyogenic abscess or may remain a cyst. The size of the abscess or cyst varies, occasionally it attains several centimeters in diameter. The orifices of Bartholin's glands are occasionally just visible as red spots (gonococcal maculae) In ancient infections Bartholin's glands remain indurated

SYMPTOMS The symptoms of gonorrhea are classed as acute and chronic. Many women during acute gonorrhea notice a slight burning on urination, perhaps an increase of a vaginal discharge, and discomfort. These symptoms are experienced frequently by most women, however, and are usually inconsequential. Other women have had no unusual symptoms and are unaware that anything is wrong until salpingitis develops A few women have acute symptoms, comprising definite burning on urination, frequency, vaginal pain, itching and leukorrhea

Chronic gonorrhea of the external genitalia of women, as a rule, does not cause symptoms In a few women, however, the symptoms of chronic gonorrhea of the internal genitalia never seem to subside There are leukorrhea and urinary symptoms and a continuance of the active and infectious disease. In a few cases cysts of Bartholin's glands may cause local inconvenience; recurring abscesses of Bartholin's glands cause local pain, swelling and redness, recurrent burning on urination, and cystitis Sterility may be the complaint caused by a gonorrheal cervicitis However, sterility does not often occur, for many women who have chronic gonorrhea bear children normally.

After long periods without symptoms, there may be exacerbation of the infection, abscess of Bartholin's glands, cystitis, salpingitis or arthritis.

EXAMINATION In the acute stage there are general swelling and redness of the genital mucosa accompanied with a purulent discharge from the urethra and cervix Results of examination of those who have chronic gonorrhea may be negative, or there may be pus expressed from Skene's glands.

Zondek tests are often stronger than normal in a live hydatid. Diagnosis is established by microscopic examination of the products of uterine curettage

Malignant Tumors. Chorionepithelioma, a rare complication of a rare disease, the hydatid mole, may follow abortion, full term pregnancy or ectopic pregnancy, or may occur as a tumor of the testicle. In men it exhibits the same degree of malignancy and high urinary titer of hormones (Aschheim-Zondek, Friedman and frog tests) that are observed in women. Metastasis in chorionepithelioma is widespread and early The common sites of metastatic lesions are the lungs, vagina and brain

The appearance of a vaginal lesion may be the first indication of a chorionepithelioma. After an abortion, full term pregnancy or ectopic gestation repeated or continued bleeding usually is due to retained placental or decidual tissue, and curettage is performed If bleeding recurs after curettage and is accompanied by a rising titer of chorionic hormones in the urine, the diagnosis of chorionepithelioma can be made from these symptoms. The diagnosis is established by microscopic examination of a metastatic nodule or the primary tumor.

THE UTERINE (FALLOPIAN) TUBES

A normal uterine tube is about 4½ inches (11.4 cm) long and runs in the broad ligament along its top or free edge from the uterus to the ovary

CONGENITAL MALFORMATIONS The uterine tubes develop from the mullerian ducts, along with the uterus and the upper part of the vagina In a grave defect, such as complete nonunion or marked inhibition in the development of the mullerian ducts, the uterine tubes are likely to be rudimentary In the absence of the uterus, or in the presence of completely double uterus or rudimentary uterus, the uterine tubes are hindered from their normal development.

Double Fimbriae This condition is not rare and is inconsequential, causing no symptoms

Congenital Occlusion. Congenital occlusion of the uterine tubes is accompanied by retarded uterine development (hypoplasia).

Absence of Uterine Tube This malformation is rare. It is usually due to aplasia of an entire mullerian duct and is evident in the resulting type of uterine deformity, uterus unicornis. In this condition the entire uterus, cervix and upper part of the vagina are formed from one mullerian duct.

Absence of one mullerian duct, with consequent absence of one tube, may be accompanied by absence of the homolateral ovary and kidney.

Rudimentary Uterine Tube. This is also rare except in the presence of rudimentary development of the whole mullerian duct

Infections. Infections, termed salpingitis, are the most important lesions of the uterine tubes. They are significant, not only because of their effect on the patient's health, but also because they frequently produce permanent tubal occlusion and sterility

The inflammatory diseases of the uterine tubes conform to certain definite types, of which the commonest are those due to (1) gonorrhea, (2) pelvic abscesses, (3) tuberculosis, (4) puerperal infections and (5) appendicitis Other less common varieties are associated with systemic infection. Not all tubal infections are discussed here.

1. ***Gonorrhea.*** Gonorrhea is primarily an infection of the mucous membrane of the urogenital tract of men, women, and girl children. In women of the child-bearing age the characteristic type of infection occurs in the *uterine tube* It is for this reason that gonorrhea in women is discussed with diseases of the uterine tubes, the epithelium of the uterine tubes offers little resistance to the gonococci.

Since the advent of chemotherapy and antibiotic therapy the following sequence of events occurs only when the infection exists without the benefit of the use of these drugs.

OCALIZATION. The vaginal epithelium in children, in women during pregnancy, in senile women is thin, its secretions are but slightly acid, and it offers slight ance to the gonococci

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DIAGNOSIS. The presence of gonococci in these secretions, demonstrated by smears, by cultures or both, *establishes the diagnosis.* However, in many cases the diagnosis is impossible. The gonococcus is so deeply buried in glands and epithelium that it is inaccessible. Positive results on smears or cultures may be obtained during or near the menstrual periods

a. **Gonorrhea of the Uterine Tubes** (*Salpingitis*). Salpingitis occurring at the time of a menstrual period or after childbirth or miscarriage may be the first manifestation of gonorrhea of the uterine tubes. Many times salpingitis has followed intracervical or intra-uterine instrumentation.

SYMPTOMS During a menstrual period complicated by salpingitis the dysmenorrhea, if present, is increased, the period is *prolonged*, and the flow more profuse After the period the pain continues and increases. Micturition is painful. Leukorrhea, fever, backache, *painful defecation, anorexia, nausea and often vomiting* are not unusual.

In some instances the infection is severe, and if proper antibiotic therapy is not given, recovery may be delayed by *formation of abscess and exacerbations of* symptoms during successive menstrual periods Acute abscesses occur in the uterine tubes or the ovaries (pyosalpinx, ovarian or corpus luteum abscess), in the pelvis (pelvic abscess), Bartholin's glands, urethral glands or perirectal tissues However, if antibiotics are administered, these complications can be minimized or prevented

One attack of acute salpingitis, even without treatment, does not necessarily indicate that more attacks will follow. The patient may recover completely or partially without treatment In the severe infections complete recovery may be assumed when there is restitution of normal childbearing and menstrual functions. The internist is in no hurry to advise surgical operation on a young woman who has acute or subacute salpingitis simply because recovery is slow.

EXAMINATION The abdomen may be moderately distended, and there is bilateral tenderness in the suprapubic region. On occasion the tenderness is limited to the right lower quadrant, requiring a differentiation from acute appendicitis

Muscle guarding is infrequent in salpingitis. Often a mass is demonstrable early in the course of the disease

In many patients who have acute salpingitis a pelvic examination reveals evidence of gonorrhea of the external urogenital tract On bimanual palpation the characteristic findings are bilateral tenderness and increase in the local temperature of the parts. The pelvis is generally and bilaterally sensitive, and movements of the cervix and uterus cause pain. Often no masses are palpable at this stage. There may be only a general sense of resistance and tenderness through the whole pelvis.

There may be found *thickening of the ovarian capsule* and adhesions between the ovary, uterine tube and surrounding organs. Perioophoritis, ovarian abscess, tubo-ovarian cysts, pyosalpinx and tubo-ovarian abscesses are common findings

Thickening of the ovarian capsule and its adhesions causes impediment of ovulation by ovarian adhesions and may result in graafian follicular cysts If so, when the graafian follicle ruptures, virulent gonococci may penetrate the corpus *luteum* and cause a *corpus luteum abscess*

The adnexa may be adherent to the posterior surface of the uterus, and intestines and omentum may become adherent to the fundus, but infection is superficial Intramural abscesses have occurred The endometrium is almost immune to the gonococcus except when traumatized.

Laboratory tests may reveal leukocytosis with an increase in the ratio of the polymorphonuclear cells. The sedimentation rate is increased

DIAGNOSIS. Positive smears and cultures for gonococcus are the only means of establishing a positive diagnosis The history and the findings on examination are usually sufficient for a clinical diagnosis.

Acute salpingitis may closely simulate acute appendicitis, tubal pregnancy and ovarian cyst with twisted pedicle, and it may resemble many other pelvic conditions also. Chronic salpingitis may simulate almost any pelvic disease. With its many pelvic lesions, chronic salpingitis often presents atypical features which may be confusing or impossible of exact diagnosis until biopsy has been made or positive culture for the gonococcus is obtained.

b **Gonorrhea in Pregnant Women.** During pregnancy gonorrhea seems to be able to produce a more serious vaginitis than when pregnancy does not exist. After the uterus has been emptied, during the puerperium, or after the first menstrual period after the puerperium, severe salpingitis often occurs.

c. **Gonococcal Vaginitis in Children.** Gonococcal vaginitis is common wherever persons who are infected with the gonococcus come into contact with girls Gonorrheal infection is conveyed by infected hands, or by infected toilet seats or other bathroom facilities Gonorrheal vaginitis may attain epidemic proportions in orphanages of girl children.

The infection causes a deep inflammation which extends through the epithelial layer into the fibromuscular tunic of the vagina. There is vulvovaginitis, and the labia minora and the inner surface of the labia majora are swollen and red. The chief symptom is a purulent vaginal discharge. There are discomfort, itching, and burning on urination

The course of the disease before the era of antibiotics and chemotherapy was most intractable and persistent. Many patients were not cured until they reached the menarche, when the infection was eliminated physiologically by the natural development of a new type of vaginal epithelium

The diagnosis is established by identification of the gonococcus by smear or culture The presence of a purulent discharge in a girl is suggestive of gonorrhea.

d. **Gonococcal Peritonitis.** An acute gonococcal salpingitis is constantly accompanied by an acute pelvic peritonitis which is limited to the pelvis and disappears spontaneously in a week or 10 days. It produces an acute general peritonitis in children and young girls which is often the first indication of gonorrhea Occasionally an acute peritonitis may arise from a chronic salpingitis General peritonitis secondary to chronic tubal infection may develop as the result of rupture and escape of infectious material from a tubo-ovarian abscess, or pelvic abscess

2 **Pelvic Abscess.** Pelvic abscesses are multilocular, and those intrinsic to internal genitalia of the female communicate with tubo-ovarian abscesses or a pyosalpinx Often they are extrinsic to the pelvic organs and are due to the collection of infected fluid from the rupture or chronic perforation of some intra-abdominal viscus

Pelvic abscesses are enumerated according to the close association and frequency of infection of the structures in and around the pelvis (1) postappendical, (2) salpingitis, (3) postoperative collection of serum or pus, (4) pelvic abscess from perforation of sigmoid or cecum, (5) postoperative hematoma or hematocele; (6) infected hematocele from rupture of ovarian cyst, (7) osteomyelitis; (8) diverticulitis of the pelvic colon, (9) chronic ulcerative colitis or ileitis and (10) puerperal infections

Pelvic abscesses may rupture spontaneously into the bladder, vagina, rectum or sigmoid They may rupture through the abdominal wall, particularly those which arise from chronic ileitis Abscesses from chronic ileitis and from puerperal infection may reach the extraperitoneal fascial planes and burrow around the bladder, between the layers of the broad ligaments, down the fascial planes of the thigh or pass upward into the perirenal fossae. A pelvic abscess may follow the urachus to the umbilicus, and may rupture and drain at that point

Fistulas follow the rupture of the abscess into the vagina, bladder or rectum.

DIAGNOSIS. The presence of gonococci in these secretions, demonstrated by smears, by cultures or both, establishes the diagnosis. However, in many cases the diagnosis is impossible. The gonococcus is so deeply buried in glands and epithelium that it is inaccessible. Positive results on smears or cultures may be obtained during or near the menstrual periods

a. **Gonorrhea of the Uterine Tubes** (*Salpingitis*). Salpingitis occurring at the time of a menstrual period or after childbirth or miscarriage may be the first manifestation of gonorrhea of the uterine tubes. Many times salpingitis has followed intracervical or intra-uterine instrumentation

SYMPTOMS During a menstrual period complicated by salpingitis the dysmenorrhea, if present, is increased, the period is prolonged, and the flow more profuse. After the period the pain continues and increases Micturition is painful Leukorrhea, fever, backache, painful defecation, anorexia, nausea and often vomiting are not unusual.

In some instances the infection is severe, and if proper antibiotic therapy is not given, recovery may be delayed by formation of abscess and exacerbations of symptoms during successive menstrual periods Acute abscesses occur in the uterine tubes or the ovaries (pyosalpinx, ovarian or corpus luteum abscess), in the pelvis (pelvic abscess), Bartholin's glands, urethral glands or perirectal tissues However, if antibiotics are administered, these complications can be minimized or prevented.

One attack of acute salpingitis, even without treatment, does not necessarily indicate that more attacks will follow. The patient may recover completely or partially without treatment. In the severe infections complete recovery may be assumed when there is restitution of normal childbearing and menstrual functions. The internist is in no hurry to advise surgical operation on a young woman who has acute or subacute salpingitis simply because recovery is slow.

EXAMINATION The abdomen may be moderately distended. and there is bilateral tenderness in the suprapubic region. On occasion the tenderness is limited to the right lower quadrant, requiring a differentiation from acute appendicitis.

Muscle guarding is infrequent in salpingitis. Often a mass is demonstrable early in the course of the disease

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tiation of genital tuberculosis from chronic salpingitis is impossible until the tissue studied histologically.

Of the various methods used to establish the definite nature of the adnexitis, rettage is the one most widely used, although exploratory laparotomy, salpingo-aphy, and culdoscopy are also occasionally employed. Curettage is occasionally llowed by exacerbation of the tuberculous process. Inoculation of menstrual blood to guinea pigs can be valuable in establishing the tuberculous nature of salpingitis.

Extra-uterine Pregnancy. The situation of extra-uterine pregnancy most mmonly is the *uterine tube,* rarely the ovary or the abdominal cavity. Ectopic station often occurs with the first pregnancy, if with the second pregnancy, or ccessive pregnancies, a period of sterility may precede the ectopic gestation

When the fertilized ovum is prevented from passing through the uterine tube. tra-uterine pregnancy results Salpingitis is the commonest cause of tubal preg-ancy, but other causes may be present, such as peritubal adhesions or a congenital rrowing Other causes of tubal obstruction are diverticula, rudimentary horn of ouble uterus and pelvic tumors

The sequence of the symptoms may be a preliminary amenorrhea or delayed enstruation followed by irregular bleeding and sudden or repeated pain. There ay have been slight anorexia and nausea, swelling of the breasts and mild pelvic scomfort. Severe pelvic pain, feeling of weakness or faintness, fainting, nausea, omiting, and vaginal bleeding, shock and collapse may develop rapidly In about in every 4 sudden collapse does not occur Patients who do not have sudden ollapse may feel only a sense of profound weakness, faintness, dizziness and capacitation In some instances the patient may suspect that she is having a mis-arriage

As the amount of blood in the pelvis increases and adhesions form, the pelvic iscomfort is increased by an exertion, defecation, and micturition.

On examination the pelvis is so sensitive and the patient in such severe shock at the ruptured tube is not palpable, blood crepitus is usually absent

In the less acute tubal ruptures examination reveals a normal abdomen On elvic examination the cervix is often softened and the uterus is soft and somewhat nlarged The characteristic feature is a soft, sensitive, cylindrical mass in an dnexal region or in the recto-uterine pouch. On rare occasions, if manipulation not considered too dangerous, the ovary on the same side may be isolated, and so, the tentative or presumptive diagnosis of unruptured tubal pregnancy may easonably be made

In tubal pregnancy, as long as the fetus or the trophoblast survives, reaction to e Aschheim-Zondek or a similar test is positive. After the fetal elements die, the eaction becomes negative unless there is a proliferative, independent growth of the ophoblast such as occurs in the presence of hydatidiform mole, or unless there is lso an intra-uterine pregnancy

A specimen of urine is obtained and examined for pregnancy hormones. If re-ults are positive, examination under anesthesia is indicated, and if the findings are onfirmed, laparotomy is performed

In the acute types of tubal rupture the *diagnosis* is established by the history and he acuteness of the onset and collapse. In the less acute type of tubal pregnancy, without acute symptoms, but with repeated attacks of moderate discomfort, the iagnosis is much more difficult The condition may simulate threatened abortion, ppendicitis, salpingitis, ovarian cyst with torsion of the pedicle, ruptured corpus uteum cyst, and a variety of pelvic and abdominal conditions.

Tumors. *Papilloma* of the uterine tube causes no symptoms It is the only com-non benign tumor of the tube Cysts in the broad ligament, remnants of the aroophoron, may be difficult to distinguish from hydrosalpinx.

The fistulas from abscesses of the pelvic organs often heal spontaneously. Fistulas from ruptured diverticula of the colon and those from chronic ileitis never heal spontaneously

In the acute pelvic abscess the symptoms are those of acute salpingitis. The fever is high, the pain intense, and the pulse rapid. In chronic pelvic abscess there may be no acute symptoms The hard mass is found on pelvic examination, made because of vague pelvic complaints

If the patient who has a pelvic abscess suddenly begins to have acute abdominal pain, with nausea and vomiting, there may have been a rupture of the abscess into the abdominal cavity with subsequent *peritonitis. The abscess should be evacuated* surgically.

Abdominal palpation discloses tenderness and perhaps a mass in the lower part of the abdomen Pelvic examination reveals a mass, and there may be fluctuation in the recto-uterine pouch The indurated adnexa may or may not be identifiable. As a rule, in the presence of a pelvic abscess, intrapelvic structures cannot be identified.

Chronic pelvic abscesses are hard and fixed masses, moderately sensitive, and situated behind the broad ligaments.

On rectal palpation the finger is insinuated higher in the pelvis than it can be through the vagina The finger can often determine the extent of the abscess, its relation to the pelvic walls, the cervix and the rectum The presence of pus is indicated by anemia, long-standing illness with the history of fever and infection, and cachexia.

3. ***Genital Tuberculosis in Women.*** The pelvic organs are usually infected with tuberculosis through the blood from distant foci such as lungs, the mediastinal or peribronchial lymph nodes, the intestinal tract, peritoneum or bones The infection occurs usually between the ages of 20 and 40 years In adolescent girls the disease often takes the form of a diffuse, miliary, tuberculous peritonitis with ascites. Aged women occasionally succumb to the disease. Genital tuberculosis is rarely contracted by coitus The uterine tubes are nearly always involved, whereas the ovaries are involved in only about a third of the cases and the uterus (endometrium) in from one half to three fourths of the cases Clinically, tuberculous salpingitis does not differ from other forms of adnexitis Almost always tuberculosis affects both uterine tubes Except for isolated instances of vulval, cervical and vaginal tuberculosis, genital tuberculosis in women means involvement of the tubes

In 1 of every 4 women who have genital tuberculosis there is active pulmonary tuberculosis. Active pulmonary lesions are therefore important symptomatically and diagnostically.

A long history of chronic constitutional and gastrointestinal symptoms accompanied by menorrhagia, dysmenorrhea, amenorrhea, intermenstrual spotting, leukorrhea, sterility, and recurring pelvic and abdominal pain is suggestive of genital tuberculosis. If these symptoms are associated with pulmonary manifestations of tuberculosis they are more significant

If on *examination of a virgin there are found pelvic* lesions indicative of chronic salpingitis, adnexal mass, induration, fixation of the adnexa and unexplained tenderness, a presumptive diagnosis of genital tuberculosis is made

In a married woman, absence of signs of gonorrhea and no reasons to suspect gonorrhea would support the diagnosis of tuberculosis if there was present evidence of a chronic salpingitis.

In the presence of an active pulmonary tuberculosis, a pelvic inflammatory disease may be of tuberculous origin If the cervix is involved, biopsy may reveal the presence of tuberculosis In the absence of active pulmonary lesions the differ-

Small follicular cysts do not cause symptoms. A large cyst or many small cysts in the ovaries may produce pelvic pain, menorrhagia and at times amenorrhea On pelvic examination the ovaries are bilaterally enlarged, tender and cystic. The diagnosis thus is strongly suspected A definite diagnosis may require time and finally histologic studies.

Corpus Luteum Cysts. These cysts may develop rapidly. Once formed, they may remain for a long time.

Pain which is not characteristic and menstrual disturbances are present when there are corpus luteum cysts The menstrual disturbances are the usual ones, menorrhagia, metrorrhagia and amenorrhea. At times these cysts rupture and permit of severe intra-abdominal bleeding, and the symptoms then produced simulate those of abortion or tubal pregnancy Hematomas contained within the cysts, in the presence of salpingitis, may become infected and form abscess (corpus luteum abscess).

Lutein cysts are usually bilateral and multiple, and constitute a mass that may be up to 4 inches (10.2 cm) in diameter. Ovarian cyst is about as accurate a diagnosis as can be made

Cystomas. The ovarian cystomas comprise the simple cystomas, the serous' cystadenomas, and the pseudomucinous cysts. These cysts are histologically benign tumors.

The simple serous cystomas may be unilateral or bilateral. They are unilocular cysts with thin walls and contain clear fluid The serous cystadenomas are filled with a watery fluid The pseudomucinous cystadenomas are multilocular. The contents of these cysts are a thick, glairy, gelatinous material that contains pseudomucin.

The *serous cystadenomas* may occur unilaterally or bilaterally. They attain great size. In the presence of pseudomucinous cyst, fatal results may follow dissemination of pseudomucinous material in the peritoneal cavity during a surgical operation. This condition is known as *pseudomyxoma peritonaei*. There is a rapidly accumulating ascites

On examination the cystomas are found as bilateral, lobulated cystic tumors. On palpation these cysts are not uniform; some portions of the surface are very soft and collapsible, owing to low tension of the enclosed fluid, others are hard and resistant, giving the impression of almost complete solidity, owing to the glandular growth in the wall of the cyst

These different cysts cannot be said to be benign or malignant until seen and examined microscopically.

Tumors Arising from Embryonic Rests of Cells. The tumors of the ovaries which arise from embryonic rests are the granulosa cell tumors, arrhenoblastoma, adrenal tumors of the ovary, dysgerminoma and the Brenner tumor

The *granulosa cell tumor* is a malignant, feminizing, hormone-producing tumor. It causes precocious sexual development in girls and rejuvenation in older women. These tumors may occur at any age but are commonest in childhood They may attain a large size, filling the abdomen Generally they are from 4 to 5 inches (10 2 to 12.7 cm.) in diameter. The most constant feature of the histologic structure is its variability, which can be identified only by an expert pathologist

A precocious sexual development is characteristic The sexual changes are more noticeable before puberty and after the menopause than at intermediate ages In childhood granulosa cell tumors cause precocious development of the reproductive organs, and menstruation begins in a normal fashion but at much too early an age.

After the menopause a granulosa cell tumor causes sexual rejuvenation The breasts become full, the vagina and external genitalia resume the features of mature sexual life The uterus returns to its normal size and menstruation is resumed. It may be irregular or periodically normal. If, therefore, hyperplastic endometrium is obtained on biopsy in the search for the cause of postmenopausal bleeding, a granulosa cell tumor is present if the patient has not received estrogen therapy.

Carcinoma of the uterine tube occurs both primarily and secondarily. Primar carcinoma of the tube is rare; secondary carcinoma is common in abdominal an pelvic carcinomatosis.

Carcinoma is usually situated in the middle or outer third of the tube. The gros appearance of the tumor depends on its size and the situation of and patency of th fimbriated extremity of the tube. If the fimbriated extremity is open, peritonea implantation is the rule, leading to ascites, carcinomatosis and death. Metastasi and dissemination occur early and are widespread

The first symptom of carcinoma of the uterine tube usually is pain. Pain i followed by a vaginal discharge which is bloody. The first symptom may b abdominal enlargement due to ascites and peritoneal carcinomatosis.

The pain may be dull with sharp exacerbations. It may be as severe as the pai in a tubal abortion but without shock because rarely is there any internal hemorrhag in tubal cancer, and hence there are no syncope and shock. Menstrual irregularitie of all types occur, the commonest being metrorrhagia and menorrhagia.

Secondary carcinoma of the uterine tube is commoner than primary carcinoma Being usually metastatic, it generally first starts in the tubal wall as discrete nest and then extends into the tubal lumen.

The diagnosis of carcinoma of the uterine tube is made from histologic studies

THE OVARIES

The ovary lies longitudinally or obliquely against the outer wall of the pelvis. From its upper end proceeds the suspensory or infundibulopelvic ligament and from its lower end the utero-ovarian ligament. The normal graafian follicles and corpus luteum can be palpated on the surface of the ovary in thin women.

Congenital Malformations. Absence of one ovary is rare, but when it occurs, the absence is due to complete agenesis of one urogenital fold, and the corresponding kidney is also absent In the absence of one urogenital fold in the female the uterus is unicornous, derived from only one mullerian duct. The uterine body is fused with the single uterine tube The other uterine tube is likewise absent.

In the ovaries when there is a follicular agenesis, there is no follicular epithelium. The uterine tubes, uterus and breasts are underdeveloped The axillary and pubic hair is absent or scanty and the external genitalia are infantile in type. The urinary gonadotropins are elevated, as they are after menopause The 17-ketosteroids are low. Often there are many other and severe congenital and acquired anomalies. The absence of genital development is often the least of the disabilities present as the result of congenital malformations. In these patients the ovarian failure is a basic lesion in the ovary itself

Tumors. Tumors of the ovaries are often complex structures histologically and may defy the knowledge and ingenuity of the pathologist to classify them. They may be benign or malignant, or they may consist of immature male gonadal elements which secrete male hormonal substances which produce masculine secondary sex characteristics Grossly, on examination by physical means, they are found to be either cystic or solid in structure, benign or malignant in nature. Whether or not they are cystic or solid does not separate them structurally into benign and malignant groups, for both cystic and solid tumors of the ovaries may be found to be malignant.

Retention Cysts. These cysts are benign but may become malignant and originate serous cystomas and cystadenomas. Retention cysts arise from occlusions of germinal epithelium. The germinal layer of epithelium may be present only in the fissures that separate lobulations of the ovary. Cysts are formed when this germinal epithelium is occluded by adhesion

Follicular Cysts. The follicular cysts may originate in normal ovaries or as the result of an inflammatory thickening of the ovarian capsule which prevents rupture of the follicle. Follicular cysts are 1⅕ or 1⅗ inches (3 or 4 cm.) in dia eter and occur bilaterally.

Of the secondary carcinomas of the ovary, the *Krukenberg tumor* (fibrosarcoma ovarii mucocellulare carcinomatodes) involves both ovaries and is usually preceded by or accompanied by a neoplasm in the stomach, intestinal tract or breast. As a rule, there is a history of a previous neoplasm in one of these regions. The original focus of the growth may not have been suspected, however, and it is not discovered until the pelvic tumor is discovered Krukenberg tumors usually occur in women between the ages of 20 and 60 years

Not all secondary ovarian carcinomas have their primary origin in the alimentary tract For instance, carcinoma of the breast may metastasize to the ovary. At least 7 of each 10 of the secondary ovarian tumors are of the same cell type as the original growth.

The symptoms of secondary ovarian carcinoma may be those of the primary growth in the stomach, intestine or breast or may be referred to the pelvis or to an enlarged abdomen On pelvic examination there are bilateral solid ovarian tumors. Often there is ascites Bilaterally enlarged ovarian tumors in a woman who has a tumor of the breast, stomach or intestines are diagnostic The original tumor may have to be sought for after the bilateral ovarian tumors are found The prognosis is generally hopeless

Tumors Arising in the Ovum (Teratomas). Teratomas are embryonic tumors which are characterized by containing one or all of the three primordial layers of tissues ectoderm, mesoderm and entoderm Teratomas are organized to varying degrees into special organs such as hair, teeth, skin, bone, cartilage, thyroid, intestine and other organs.

The younger the ovum is, when the growth disturbance takes place, the more nearly totipotential its cells are and the more capable of producing all their tissues The older the ovum, the more specialized the cells and the less capable they are of producing a variety of tissues and thus the origin of dermoid cysts (MacCallum).

Dermoid cysts are simple forms of teratomas. Teratomas and dermoids may be found anywhere in the body but have a predilection for the ovary

Malignancy is common in teratomas, in dermoids it is relatively rare.

Struma Ovarii. The ovarian tumors which contain thyroid tissue are termed struma ovarii These are in reality ovarian teratomas

Struma ovarii is distinguished by its ability to produce symptoms of hyperthyroidism before removal and occasionally after removal of the thyroid gland. The tumor has a high iodine content This tumor is aberrant endocrine tissue and hence secretes hormones

The chief symptom is an enlarged and uncomfortable lower part of the abdomen At times there may be mild abdominal pain Much of the abdominal enlargement is due to the ascites which is often caused by peritoneal implantations of the tumor. On examination there may be the signs and symptoms of hyperthyroidism accompanied by ovarian enlargement

and myxedema Generally the prognosis is excellent unless the tumor is malignant.

Connective Tissue Tumors of the Ovary. Fibromas and sarcomas are rare tumors of the ovaries They may occur at any age, although sarcomas are found most commonly in younger persons, even in children; fibromas, in adult women These tumors may attain 4 to 6 inches (10 2 to 15.2 cm) or more in diameter. They occur bilaterally, and are often associated with ascites and hydrothorax.

Fibromas differ from sarcomas by remaining within the limits of the ovary There are varieties in appearance and color of fibromas and sarcomas, but the characteristic gross difference in these tumors is that sarcomas are much more vascular than

On palpation the tumor is smooth and may be firm; often it contains cystic portions, but usually it gives the impression of a solid mass.

The diagnosis of a granulosa cell tumor is established by the presence of an ovarian mass, sexual precocity or rejuvenation, and the histologic *presence of cells* suggesting or resembling granulosa cells of primordial follicles of the ovary.

In children the other causes of sexual precocity are cortical adrenal hyperplasia or tumor, pituitary tumors and disorders of the hypothalamus. The removal of a cortical adrenal tumor is followed by disappearance of precocious sexual development. The temporary sexual precocity does not seem to have any *permanent ill* effect.

The *arrhenoblastoma* is a malignant ovarian tumor associated with the defeminization or masculinization of a woman. It is to be differentiated from adrenal cortical hyperplasia or tumor of an adrenal gland. Arrhenoblastoma is always to be considered as a malignant tumor, but as in the malignant granulosa *cell tumor*, recurrence may be very slow in developing

At first there occurs a slow process of defeminization of the woman. Then follows the development of masculine traits such as hypertrichosis, growth of beard, increase in length of clitoris, deepening of the voice, and development of masculine contours.

Adrenal tumors of the ovary are malignant tumors and are said to be histologically like cortical adrenal tissue, resembling the hypernephroma type of cell. The histologic, biologic and clinical resemblance between cortical tumors of the adrenal gland and arrhenoblastomas indicates an embryologic kinship

Cortical adrenal tumors masculinize females and cause sexual precocity in boys In all cases of manifest sexual changes, precocity, sex reversal or rejuvenation, the ovaries, adrenals, pituitary and hypothalamic disorders (see Chapter 14) are studied

The *ovarian dysgerminoma* is usually malignant It does not exert any influence on sexual development or the hormonal balance. It is the homologue of the seminoma, an embryonal carcinoma, a common testicular tumor. The dysgerminoma is supposed to arise in rests of the undifferentiated mesodermal cells of the primitive ovary before these cells develop either male or female characteristics This tumor has a tendency to occur in patients who have sexual maldevelopment such as hypogenitalism and hermaphroditism

Dysgerminomas may be rather large tumors and often bilateral. They are hard, elastic, at times nodular, and may be accompanied with ascites Some of these tumors are malignant, others are possibly benign

The *Brenner tumor* is considered to be a benign tumor It is a rare growth which secretes no hormone When of small size, it appears as a solid mass but when large, it may appear as a cystic adenoma, with large nodular masses on its surface. The Brenner tumor is diagnosable only by histologic study.

Carcinomas of the Ovaries. Ovarian carcinomas occur as both solid and cystic tumors. The solid carcinoma of the ovary develops directly from ovarian tissue. The cystic carcinomas develop from some other ovarian tumor, such as a papillary cystadenoma. Epithelial tumors develop in the dermoids and the teratomas of the ovary.

Solid carcinomas of the ovary begin on the surface of the ovary, involve the whole gland, and extend to involve surrounding structures, the broad ligaments, pelvic floor and peritoneum. They metastasize freely, especially to the lungs. They do not cause any early symptoms. The patients first complain of abdominal enlargement, which is due mainly *to ascites*

On examination carcinoma of the ovary is difficult to palpate, even when fairly well developed In a woman in whom bimanual examination is difficult an insensitive ovarian carcinoma is often impossible to feel

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fibromas. In sarcomas secondary growths in the pelvis or throughout the peritoneal cavity, on the intestine and in the omentum, may be present. The pelvis may contain bloody fluid if implantations are present.

Sarcomas are among the most malignant of ovarian tumors. Because they rarely produce any symptoms until they are well developed, cures are rare. Metastasis and direct invasion, with peritoneal implantation, are the common modes of extension.

The diagnosis of both fibromas and sarcomas is made by microscopic study of the tissue The presence of a solid, insensitive, freely movable, hard mass in the region of the ovary suggests a *fibroma*. If ascites is present, the diagnosis is more nearly certain The *diagnosis of sarcoma* of the ovary is more difficult than that of fibroma, because the tumor is softer and may be confused with other ovarian tumors.

Complications of Ovarian Tumor. *Twisting or torsion of the pedicle* of an ovarian tumor is associated more commonly with dermoid cysts, fibromas and cystomas than with other types of tumor If the rotation occurs suddenly, it instantly produces unbearable pain, nausea, vomiting and shock. When the twisting develops slowly, there are often recurring attacks of moderate pain, which may become more severe and constant as the twist becomes tighter

Examination in the case of twisted ovarian pedicle reveals an abdomen that is acutely tender and, in the later stages, rigid. The ovarian mass on pelvic examination usually is palpable The final diagnosis may not be made until laparotomy is performed

Rupture of ovarian cysts is common and occurs in cysts that have thin, distended walls There is usually a history of a fall There may be abdominal discomfort, and often there is severe pain In an occasional instance a cyst may rupture and drain through the vagina without serious consequence.

Free perforation is common in endometrial and corpus luteum cysts. Peritoneal irritation or peritonitis develops if the contents of the cyst are chemically irritating or infected

Intra-abdominal hemorrhage may follow the rupture of an ovarian cyst and produce severe symptoms very similar to those of rupture of ectopic pregnancy. Hemorrhage of varying degrees may occur in connection with ovulation and the rupture of a normal graafian follicle, and this tends to recur with subsequent ovulation

CHILDBIRTH INJURIES

Mechanical Injuries. Mechanical injuries which occur as the result of pregnancy or childbirth commonly involve the reproductive organs, the urinary organs and their supports, and the abdominal wall. Mechanical injuries which involve the supporting structures in the back or the bony pelvis are less frequent.

Mechanical injuries of the reproductive organs and the supporting structures result in lacerations of the perineum in varying degrees (first degree, second degree and third degree), or complete perineal tear, rectocele, enterocele, cystocele, relaxation of vesical sphincter, descensus and retrodisplacement of uterus, prolapse of uterus, cervical laceration and infection, prolapsus of vagina, inversion of uterus, and rectovaginal, vesicovaginal and ureterovaginal fistulas. Some of these injuries, such as relaxation of the vesical sphincter, can be discovered only by special examination (endoscopic examination), although they may produce characteristic symptoms.

Rectocele is a hernia of the rectum into the vagina. It is due to stretching or tearing of the rectovaginal septum. Abdominal and rectal pressure causes the rectum to bulge into the vagina through the weakened rectovaginal septum

Enterocele is located in the recto-uterine pouch and is a hernia through the pelvic floor. It may contain small or large intestine, omentum, or the a

Cystocele is a protrusion or partial hernia of the bladder due to a stretching and relaxation of the vesicovaginal septum. The intra-abdominal pressure and the weight of the bladder and intestine cause the bulging of the bladder into the vagina

Descensus of the uterus can occur only when the broad ligaments and uterosacral ligaments are sufficiently relaxed to allow it. Uterine descensus may be of various degrees of severity; its end stage is prolapse.

Prolapses of the uterus are of three degrees. In *first degree* prolapse the cervix descends to the ischial spines; in a *second degree* prolapse the cervix appears at the vaginal orifice; in a *third degree* prolapse the whole uterus is extruded from the vagina Third degree prolapse and procidentia are synonymous

Prolapse of the vagina occurs in women in whom the vaginal wall lacks adequate support or in whom the supporting structures were so frail that prolapse was inevitable.

Vaginal fistulas are vesicovaginal, ureterovaginal, vesicocervicovaginal, urethrovaginal, or other combinations The commonest type is the vesicovaginal with urinary incontinence. All such fistulas are rare

Injuries to the Cervix. Many parous cervices show unhealed areas round the external os, infection and lacerations which may be only partly healed. The lacerated and infected cervix may be big, boggy and heavy and thus may increase the weight of the pelvic organs. An unhealthy cervix produces annoying vaginal discharges, dysmenorrhea, pelvic pressure, backache and urinary frequency.

Injuries to the Uterus. The commonest endometrial disorder from childbirth is an endometritis as the result of puerperal infection or retained placental tissue. Such an endometritis may become chronic The commonest permanent change in the uterus, however, is chronic subinvolution

Injuries to the Urinary Organs. A discomfort in the pelvis or in either iliac fossa may be due to a urinary lesion, probably in the ureters or the renal pelvis as a consequence of parturition Urologic examinations are required for confirmation of urologic disease to account for the postpartum urinary symptoms.

Injuries to the Abdominal Wall and the Pelvis. The *abdominal wall* is stretched during pregnancy and there may remain diastasis recti and hernia—femoral, inguinal or umbilical—which were created or made worse by gestation

The coccyx is frequently traumatized, a condition which is manifested by local symptoms

The *supporting structures* of the pelvis may be injured by a strain of the ligamentous structures Some of these injuries are the result of the unnatural postures assumed, for instance, the extreme lordosis from marked increase in the abdominal weight

Symptoms of Childbirth Injuries. A sense of pressure in the pelvis and a feeling as though the pelvic organs were protruding into the vagina, while the patient is standing, are common complaints Backache, fatigability, nervousness, irritability, lack of strength and energy, and constipation are not necessarily manifestations of birth injuries of the pelvis

Leukorrhea and urinary frequency are common symptoms of a childbirth injury In cystocele and prolapse there is a partial hernia of the bladder which prevents complete emptying of the bladder by urination and gives rise to subsequent infection and cystitis. Urinary symptoms vary from frequency that accompanies cystocele and prolapse to partial incontinence due to an injury of the vesical sphincter. Partial incontinence manifested by the loss of a few drops of urine on laughing heartily, coughing, sneezing, quickly flexing the body or lifting is a very common complaint.

Complete incontinence is the result of a vesical fistula or destruction of urinary control A constant dribbling of urine, while standing, in a woman who can hold the urine while lying down and can empty the bladder normally when it is filled, often indicates a ureterovaginal fistula.

Anal incontinence may be due to a third degree tear, even though it was repaired at the time, or may be due to a rectovaginal fistula.

Menorrhagia occurs in patients who have chronic subinvolution of the uterus, endometritis, or pelvic congestion following mild degrees of childbed fever. Childbed fever may produce tubal obstruction, endometritis, cervicitis and commonly sterility.

Dysmenorrhea following childbirth injuries is usually a continuation of that which has always been present prior to gestation. In rare instances it may be due to stenosis caused by cervical scar or to uterine misplacement.

STERILITY

CONSTITUTIONAL FACTORS IN MEN AND WOMEN. Constitutional factors which produce sterility include chronic infections, excessive use of drugs, gastrointestinal disorders, lack of physical exercise, obesity, protein or vitamin deficiency, anemia, endocrine diseases, fear, failure to relax, and anxiety or any other conditions that impair the health.

Female Sterility. Sterility is *primary* in the female if she is given adequate opportunity and does not conceive In *relative sterility* the ability to conceive is lessened but not absent. In *one-child sterility* the woman is sterile after bearing one child.

The consensus is that if conception does not occur by the end of one year of married life a couple may be considered unfertile. However, in practice it is far better to wait for at least 2 to 3 years before investigation than it is to begin investigation and treatment with the accompanying nervous tension associated with these procedures

The period of maximal fertility in women is between 18 and 30 years of age Men may retain their fertility much longer than women

The menses need not be regular in order for the ovaries to produce normal ova. If the menstrual periods occur, although in time they may occur irregularly, and if there are present cyclic changes in the cervical mucosa, it generally can be assumed that ovulation is proceeding normally. If there can be demonstrated changes in body temperature during the menstrual cycle, excretion of pregnanediol in the urine, changes in the hormone content of the blood and urine, and cyclic changes in the vaginal mucosa, ovulation is assuredly proceeding normally

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Dyspareunia may be a factor in sterility only when it prevents delivery of the sperm into the vagina It may be due to a variety of lesions imperforate *hymen*, rigid hymen; narrow vaginal orifice following infections, spasm; operative or obstetric scar; absence of vagina or other congenital defect. In the absence of the vagina the urethra may be injured in attempts to use it as a *copulative organ*

Cervicitis rarely causes sterility. Cervical stenosis, polyps or tumors may cause sterility The diagnosis of cervical stenosis is based on finding, by means of the uterine sound, a very small cervical orifice or an unusually narrow cervical canal The stenosis is frequently situated at the internal os.

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Ovarian failure may be due to congenital defects in ovarian development or may result from fundamental and general endocrine dysfunction The cause of ovarian failure may be a complete agenesis of the follicular epithelium which results in absent ovarian function If the congenital defect is limited to the ovaries, there is lack of development of the breasts, external genitalia, vagina, uterus and uterine tubes and consequently no menstruation. The uterus is very small. The ovaries cannot be felt at all. The diagnosis of follicular agenesis, however, cannot be made without histologic examination of the ovaries. Agenesis of the follicular elements is not always complete. Menstruation may occur a few times each year. Pregnancy is not likely to take place in such women.

A common cause of sterility is *obstruction of the uterine tubes.* The common cause of obstruction is salpingitis, which may be gonococcal, tuberculous or puerperal. Other effective agents for closing the uterine tubes are uterine retrodisplacement, uterine myomas, ovarian cysts, parovarian cysts and congenital occlusion of the tube

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volume, however, vary considerably and volumes from less than 2 ml. to more than 7 ml. may be normal. Very small amounts of semen may mean occlusion of the spermatic ducts.

Normally the *semen is thick and viscid* when ejaculated. It should liquefy readily, however, and be fluid *within less than half an hour. At least one half of the spermatozoa should be actively motile* after 2 to 10 hours.

Brown has made some investigations of male seminal fluid with a view to determining whether or not modification in the character of this fluid or increase in its amount might serve to protect the spermatozoa over a longer period of time and make more likely the contact of the sperm cell with the ovum. Man normally produces about 120,000,000 spermatozoa for each milliliter of fluid, or approximately 450,000,000 in the average ejaculate. A donor may produce a total of 30,000,000 to 50,000,000 spermatozoa every 24 hours daily over a considerable period. When it is realized that only one spermatozoon can impregnate the ovum, the tremendous factor of safety involved becomes apparent These studies lead to the conclusion that such influence as the glandular secretions of the male have on the spermatozoa cannot be further increased by the addition of fluid to the normal ejaculate

If more than 1 in every 5 spermatozoa are found to be abnormal, it is evidence of impaired fertility

A *decrease in the normal number of spermatozoa* is one of the commonest causes of low fertility. Spermatozoa counts of less than 60,000,000 per milliliter are inadequate.

Absence of spermatozoa in the semen results either from failure to produce sperm (aspermia) or from mechanical blockage of the seminal ducts. Congenital abnormalities of these structures are hypospadias, absence of the vasa deferentia, epididymides, seminal vesicles or ejaculatory ducts, imperfect union of testis and epididymis and congenital stricture of the vas deferens

Lack of spermatogenesis may be due to the various types of pituitary disease or to destruction of the germinal epithelium of the testis from inflammatory lesions such as orchitis of mumps, or tuberculosis, or to failure of normal testicular development as in cryptorchids

Functional Impotence. Functional impotence of the male may be due to in-[illegible] because of fear of the sexual act, fear of having children,
[illegible] the sexual act normally. Worry

It is well for the diagnostician to remember that many men and women who, after various tests and examinations, have been declared sterile, nevertheless have enjoyed rearing their own families despite the grave predictions to the contrary.

DERANGEMENTS OF SEX LIFE

The consultation is a solemn moment to the patient, man or woman. Under its influence patients find themselves confessing to the physician and asking for help which might well be sought from a minister of the gospel. When a patient is in this [illegible] can well listen and by *listening he is practicing* sound morality
[illegible] physician's affair to mend the patient's
[illegible]gularities as to encourage him to stop drinking himself to death Sexual irregularities are never normal sexual behavior.

Description of what should be considered a normal sex life can only lead to hopeless disagreement not only with one's peers but even with one's self. *It is not* the prerogative of the physician to outline the normal sex life to men and women, for the sex impulse is a normal appetite, as variable as any that can be imagined The physician is never afraid to hold up to his patients the frank ideals of a cleaner life than it would seem possible *for some of them to aspire to.* The strictest morality that can be imagined must always be outlined as routine behavior. In time delight

will come to those who give such advice; for often a responsive glow, a determination to be better, will be aroused in the most unpromising material

Morally upright and profoundly religious mothers may have read certain books about The Things Women Should Know About Their Sex Life If such a woman has not experienced an orgasm, she may inquire of the physician the reason for her lack of such an experience.

In answer to such a query it should be briefly but clearly stated that in women orgasm is a nervous reaction based on the presence of healthy reproductive organs and psychic response. It is dependent too on normal pituitary and ovarian function. If desire and orgasm have been developed without frustration, they continue irrespective of the presence of the ovaries or uterus. Even though these reactions have not been attained, if normal genital organs are present, reproduction may be possible, for there are many women who have never experienced an orgasm who have large families. It is therefore clear that while the orgasm is desirable, it is not necessary for breeding in women For the physician to enter into a psychiatric cross-examination of such a woman is nothing short of bestial brutality for such questioning is sure to offend her finer sensibilities

The removal of the ovaries shortens the span of sex life by altering the physical character of the external genitalia and the vagina. Women become indifferent sexually and have less orgasm after menopause

SEXUAL OFFENCES

The physician is consulted in regard to two types of sexual offence The first is a mental disturbance of which the crime is only a manifestation These crimes consist of repeated indecent exposure, indecent assaults upon children, lewd and libidinous practices, and the criminal acts of sadism and masochism.

The second group are deliberate sexual crimes by persons in a sane though perhaps morally degraded frame of mind Rape, incest, and sodomy and bestiality are the common offences

Rape. Rape is unlawful carnal knowledge of a woman without her consent "Unlawful" implies that there is such an act as a lawful carnal knowledge of a woman by force "Carnal knowledge" is "the slightest degree of penetration of the vulva by the penis" Penetration proper through the hymen is not necessary to the act. When the hymen is already deflorate, ruptured by previous penetrations, a great deal depends on the girl's character and bearing, the substance of her story, the condition of her clothing, and the presence of even trivial injury to any part of the body.

Evidence of a forceful assault freshly committed will be clear. There will be bruising, scratching, or tearing of the vulva or hymen which may still be bleeding

It is possible that the only proof of penetration will be a vaginal smear of seminal fluid For this reason a swab or smears should always be taken The emission of seminal fluid is not essential to the proof of carnal knowledge but its demonstration may provide proof of penetration.

The development of gonorrhea or of pregnancy in a woman after alleged rape may sometimes be used as corroborative evidence without giving it undue value, and culture as well as microscopic examination of a swab should be made if possible.

The essence of the offence is that it should take place against the desire of the woman In females less than 18 years of age the offence is carnal abuse with or without consent The age limit of 18 years may vary in accordance with local statutory law

Medical Examination in Alleged Rape. The precise time of the examination and a record of by whom it was requested are essential to record.

The raped girl or woman is shy and bewildered The story, in the girl's own words, is recorded at the time, for it will contain conversation the exact form of which may be vital. No false modesty in detail or language should be allowed to interfere with this being a full record It will gain by being graphic and tend to appear in its true light—authentic or false.

The presence of tangled, disordered hair, dirt-stained face or hands, and the condition of the clothing, tears and blood stains are recorded.

With some person present to assist, the clothing should be removed in the doctor's presence, and examination made of every part of the body. Stories of being forced against something, pinned down, gripped by the arms, kicked or punched may gain corroboration from the finding of some comparable injury in the part described

The local parts are examined for foreign hairs, to be placed in envelopes, sealed and labeled Seminal stains are smeared on slides and fixed Bruises, scratches or tears adjacent to the vulva and within it, as well as to the neighborhood of the hymen, are searched for. The state of the hymen is observed and recorded

Matted, semen-stained pubic hairs may be cut away. Dried thigh stains should be moistened with saline solution and smeared on glass slides. A vaginal swab should always be taken If the material is still wet, the peculiar odor of semen competently observed is fairly conclusive.

It is less common for the doctor to have the opportunity of examining the man accused of rape: permission must be obtained and its voluntary nature made clear before commencing The physician searches for foreign hairs on the clothing, adherent to the body or pinned under the prepuce Injury to the penis is rare, but scratches to the face or hands occur frequently (Keith Simpson).

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8

DISEASES OF THE SKIN, SUBCUTANEOUS TISSUES AND BREASTS

The skin is a protective, respiratory, excretory, heat-regulatory, absorptive, vitamin-producing and immunity-producing organ Its prickle cell layer contains the sense organs for tactile, pain, heat and cold sensations.

Layers of the Skin. The skin is composed of two main layers or parts: (1) the epidermis or cuticle and (2) the true skin. The *epidermis* or cuticle (scarf skin) is composed of the following layers beginning from the outside, the horny layer (stratum corneum); the transparent layer (stratum lucidum), the layer of flattened granular cells (stratum granulosum), the mucous layer (stratum mucosum) which contains pigment and prickle cells (prickle cell layer); the basal cell layer (stratum germinativum). The *true skin* consists of an outer or papillary layer, which contains the nerve endings and capillaries, and a deeper layer, which is largely composed of fibrous bundles. Beneath the skin is the subcutaneous connective tissue

The expanse of skin over the body is designated by topographic regions, for instance, skin of the scalp and skin of the leg These are topographic regions which normally grow hair. The regions which do not grow the regular coarse hair are designated as glabrous skin

Pigmentation of the Skin, Eyes and Hair. The stratum mucosum of the epidermis, as has been stated, contains the pigment or coloring substance, the melanin The melanin is composed of small granules which are deposited in the deep layers of the epidermis and iris and disseminated through the cells of the shafts of the hair The mucous membranes, sclerotics and some other tissues of the body contain this substance. The pigmentation of an individual is subject to change throughout different periods of life Other changes are brought about by age and exposure to sunlight and to confinement The state of feeling of the individual and the presence or absence of an oily coating of the skin likewise influence its color. In the hair the presence of air bubbles between the hair cells and the loss of melanin cause grayness of the hair, normally with aging and, allegedly, suddenly after great emotional strain.

The function of the pigmentation is to protect the individual against sunlight. The absence of pigment results in albinism with its accompanying sensitive white skin and reddened eyes which are extremely sensitive to light

Racial Colorations. Early man was a product of the tropics and subtropical regions He had brown skin, hazel to dark brown eyes and reddish brown to black [illegible]

Because of the climatic influences of the post-Glacial period the original skin pigment began to be lost, and as a result of these environmental influences and mut[illegible]
the [illegible]
to a [illegible]
in northern Europe, and thus the Celto-Slavic or Alpine coloration came into existence; while in southern Europe depigmentation was still less, leaving much of the original skin coloration and resulting in the Mediterranean complexion of swarthy

brown, with dark eyes and black hair. The continuous residence of those remaining in the tropical countries seems to have increased their skin coloration and thus resulted in the black-skinned individuals (Negroes). The Nordic white skin, the blue eyes and the blond hair still contain some of the ancient pigment. The eyes are blue because this old brown pigment is limited to the posterior cells of the iris, and the blue coloration results from refraction, whereas when the iris is viewed from behind, it is brown or dark

Freckles (*Ephelis, Lentigo*). The familiar freckles of the skin occur in those who have red hair or a tendency thereto; also in individuals who have white skins or in admixtures of white-skinned and black-skinned individuals.

A freckle is a pigmented spot, brownish in color, on the skin It is due to discrete accumulation of pigment in the rete. Freckles vary in size, in color and in number on different individuals They are made prominent by exposure to sunlight and wind. The term cold freckles is applied to those occurring on a part of the body under the clothing which is not exposed directly to the sun The origin of these freckles is the same as of those caused by direct exposure to the sun. They are less densely pigmented spots

Freckled skins are proved to be susceptible to senile keratosis and skin cancer in aging individuals.

Leukoderma. Leukoderma occurs at all ages, but among white peoples it is more common in the middle-aged than in the young. The eruption commences as a small white patch, which may enlarge and spread The disease is more frequent and extensive in hot climates and during the summer months than in other climates and seasons The lesions often occur on the face, hands, scalp and trunk, and may be symmetrically distributed The individual patches do not reveal thickening of the skin, and when they are examined for the sense of touch and pain, anesthesia is not present. When the scalp is involved, the hair on the patches turns white

The normal skin sensitivity is of importance in the differential diagnosis between leukoderma and leprosy Scleroderma may show some whitening of the areas involved, but has a distinct boardy hardness Some observers incline to the view that leukoderma is of nervous origin Actinic rays in many cases have an influence in determining its origin and localization Differentiation of leukoderma from the fully developed lesion of pinta is difficult In pinta, however, there will be other lesions of varying colors which have not yet become white (For more about pinta, see Chapter 17)

Chloasma. Chloasma is a disease the opposite of leukoderma There is a spotted increase in the normal color of the skin In chloasma the increased pigmentation has an internal origin Chloasma (or chloasma-like spots) is associated with pregnancy. There are many cases of uncertain origin Chloasma is erroneously attributed to hepatic disease (liver spots)

Acanthosis Nigricans. Acanthosis nigricans is a rare disease affecting the flexures and often resembling ichthyosis. The brown and, at times, the almost black, velvety linear overgrowth in the region of the flexures is characteristic The mucous membranes often are affected, showing warty growths without pigmentation This condition frequently is associated with widespread internal malignant disease. Besides resembling ichthyosis, acanthosis nigricans resembles Darier's disease.

Transient Coloration, Texture and Moisture. No decision concerning the color of the skin should be made until the mucous membranes of the mouth and conjunctivae have been observed Exposure to wind and weather dries, hardens and darkens the skin as well as producing other effects of less obvious magnitude. *Habitual pallor* is seen in persons who live an indoor life or who sleep in the daytime. A transient pallor of the skin may be the result of weakness of the heart action, as is observed in syncope, chills, nausea and arterial spasm. Sudden pallor, which is constant for the time being, is present when large and rapid hemorrhages

occur and when the heart fails abruptly. A slowly developing pallor is usually the result of anemia. The pallors are often described in terms of varying tints In diagnosis, however, such descriptions are worthless.

An unusual redness of the skin depends on hyperemia, the overfilling of the cutaneous capillaries with blood. Hyperemia of the skin follows a warm bath, friction of the surface of the skin, or exercise Long exposure to heat and cold and moisture produces a purplish redness of the skin of the hands which is not significant of systemic disease. *Diffuse redness* of the skin is seen in fevers, after the administration of certain drugs, and after the ingestion of alcoholic beverages. Localized redness of the skin, such as the redness of one cheek in acute lobar pneumonia and the unilateral redness of the face which attends histamine cephalalgia (Horton's headache), are observable phenomena In some *chronic alcoholics* the face is a dusky red Not all persons who have dusky red faces, however, are chronic alcoholics. The so-called dusky red face is the result of cyanosis of the skin, which is characterized by a blue or purplish tint This color arises from imperfectly oxygenated blood in the capillaries *Cyanosis* is best observed in the lips and mucous membranes and in the fingernails, if nail polish has not been used, because of the thinness and translucency of these epithelial coverings Cyanosis of the skin is caused by any condition which hinders the admission of air to the lungs, lessening the working, breathing surface of the lungs, and by any condition which interferes with pulmonary or systemic circulation Stated in more precise terms, cyanosis is due to improper oxygenation of the erythrocytes The *texture of the skin* is soft and elastic, and the skin is moist to the touch

Hyperhidrosis and Anhidrosis Excessive moisture or sweating of the skin is *hyperhidrosis,* and dryness of the skin is *anhidrosis* (see Autonomic Nervous System, Chapter 23).

Sweating of the hands or the feet attends general debility, hyperthyroidism and Raynaud's disease. It is most commonly due to nervousness. Unilateral or one-sided sweating of the head and face may be present in histamine cephalalgia (Horton's headache), neuralgia and other affections of the nervous system. Unilateral or bilateral sweating of the face may occur during a meal

Anhidrosis is characteristic of all febrile diseases, especially if the temperature is high and the rise is prolonged If the skin is injured by stretching, which alters its structure so that the cutaneous circulation is hindered, as in general anasarca, lymphedema or myxedema, anhidrosis exists as a direct result. Anhidrosis accompanies diseases in which there is an excessive loss of fluids for any reason. When renal functional activity is severely impaired, the sweat may have a urinous odor and may deposit white scales or crystals of urinary solids on the skin

Colored Sweat Yellow sweat from the biliary pigment may occasionally be present in severe jaundice. Blue, brown, yellow or red sweat has been observed in hysteria The condition characterized by colored sweat is known as *chromhidrosis.* Very rarely, bloody sweat, *hematidrosis,* is caused by capillary hemorrhage into the sudoriparous glands This condition may follow the administration of dicumarol

Dermographia. Dermographia is a condition in which tracings made on the skin leave a distinct reddish elevated mark *Dermographia alba* is the white line formed on the skin in the epinephrine test *Black dermographia* is the dark streak produced under certain conditions by stroking the skin with certain metals.

According to Urbach and Pillsbury, the black writing which appears on the skin following application of certain blunt metallic implements with moderate pressure represents not a chemical but a physical process due to the particles of the metal rubbed off by friction and remaining on the skin. While it was originally assumed that a hysterical condition was a necessary prerequisite for the phenomenon, Emdin later retracted this idea

Black dermographia is frequently observed in women who wear trinkets and

cheap jewelry of silver and gold on powdered areas. The same effect occurs on skin surfaces soiled with street, factory or mine dust.

In principle the phenomenon may be evoked on any human skin by the use of appropriate inorganic powders. There are individual differences due to variations in the moistness and oiliness of the skin. The phenomenon will appear in all persons who have dry, nonoily epidermis. The fact that the phenomenon can be evoked in the skin of a corpse conclusively demonstrates that this process cannot be regarded as a biologic reaction

History. When a disorder of the skin is present it is well to learn: (1) the duration of the disease, (2) whether there have been previous similar attacks of the eruption, (3) whether the onset of the disease was accompanied by fever, malaise, headache or generalized pains, or has been accompanied by disturbances of digestion or of the urogenital or nervous systems, and (4) whether there have been any enlarged lymph nodes

Examination. The examination of the skin should always be conducted in daylight if at all possible Of basic importance in diagnosis are detailed examination of the lesion or lesions, especially of the primary lesion, and palpation of the eruption Primary skin lesions are known as macules, papules, vesicles, pustules, wheals and hives. The secondary skin lesions are described as scales, crusts, scabs, excoriations, fissures, ulcers and scars These primary and secondary lesions may be acute or chronic. The primary lesions are of the greatest importance in diagnosis A magnifying glass used to distinguish the character of the lesion may be of great aid. The examination is performed in a definite order, beginning with the head, mouth, neck, and proceeding to the thorax, upper extremities, lower extremities and, finally, the soles of the feet and the palms of the hands It is during the examination that the examiner often is able to obtain a precise history as to whether the eruption began universally, or was widely scattered, or was grouped on the flexor or extensor surfaces of the body During the time of the examination the patient usually will mention whether the lesions began by itching, burning, hyperesthesia, anesthesia, or with pain

There are predispositions to many diseases of the skin. During childhood the common predisposing causes of skin disease are, first, those of hereditary origin, for instance, the congenital nevi and nevoid diseases, which include such disorders as ichthyosis and keratosis palmaris. Congenital syphilis may not become manifest until adolescence In later life there is a tendency toward seborrheic eczema, presenile alopecia and pigmentary disorders of the skin

Infants are subject to various infantile dermatoses and to napkin eruptions. Acne, seborrhea and hyperhidrosis occur in adolescence, whereas in advanced age epithelioma, keratosis and general pruritus develop. The relation of sex to skin disease is often important Carbuncles occur twice as often in men as in women Women are more subject than men to lupus erythematosus. Leukomelanoderma of syphilis is practically limited to women. Women suffer from contact dermatitis from the use of cosmetics, whereas men suffer more from occupational dermatitis and leukoplakia of the mouth During the winter months such diseases as psoriasis, seborrheic dermatitis, ichthyosis and chronic eczema are worse than in summer Scabies and contact dermatitis due to soap, wool and furs are commoner during the winter than in summer. During the summer months, diseases of the skin as the result of contact with various poisonous plants, hyperhidrosis, urticaria, dermatomycoses and miliaria are commoner than during the winter. In summer the insects that sting or bite and the animal parasites that suck blood are prevalent.

DISEASES OF THE SKIN

DISEASES DUE TO PRENATAL INFLUENCES

Ichthyosis. Ichthyosis is both familial and congenital. It has been thought to be due to a persistence of a fetal layer of skin, the epitrichium.

In cases of ichthyosis the secreting glands of the skin are absent. Perspiration is impossible, and the patient suffers in hot weather from vascular congestion and the lack of oil. In cold weather the extremities are susceptible to chilblains The skin is easily irritated, is hard, horny in appearance with marked dryness, harshness and formation of heavy scales. Only the flexures escape involvement. The hard masses of scales often crack across and in so doing produce fissures which become infected with pyogenic organisms.

The mildest phase of ichthyosis is termed xeroderma. All gradations between xeroderma and typical ichthyosis are observed. In the completely developed ichthyosis large platelike scales are present all over the body, but generally are worst on the extremities.

Keratosis Palmaris et Plantaris. This is a hereditary and congenital disease of the skin which affects the palms and soles and often is manifest at an early age. The lesions in appearance are like keratotic lesions on senile skin

Lichen Pilaris (Keratosis Pilaris) Around the hair follicles along the anterior surfaces of the thighs and over the outer surfaces of the arms are often observed small, firm papules that are not inflammatory These papules are discrete and at times may itch They are arranged in patches and are ill defined, and frequently some of them are capped with crusts of dried blood as the result of scratching Keratosis pilaris usually does not produce symptoms

Epidermolysis Bullosa. This is often a hereditary condition which begins in infancy and is manifested by bullae which appear after the slightest trauma. In the development of the lesions there is first redness, then wheals, and the bullae appear in less than one-half hour The patient's skin is more elastic than normal. Often there is dystrophy of the nails Epidermal cysts are of common occurrence.

Adenoma Sebaceum. This is a rare condition which even more rarely occurs alone. It is often associated with congenital nevi, fibromas, warts, rhabdomyoma and convulsive disorders and defective minds

The lesions are manifested soon after birth as small flattened tumors of the sebaceous glands on the face In the beginning the yellowish, individual lesions are small, 1 or 2 mm in diameter. Around these yellowish areas there often are dilated capillaries

Keratosis Follicularis (Darier's Disease). Morbid heredity is the only known cause of Darier's disease, which runs in families and commences in youth. There are no lesions of the mucous membrane The disorder is not associated with malignant disease Although the disease normally is chronic and slowly progressive, acute exacerbations may occur with the rapid production of fresh patches, but the general health of the patient is not impaired

This disorder is characterized by crusted dark brown papules, often coalescing in symmetric areas on the face, scalp, trunk, flexor aspects of the limbs, axillae and genital regions When the crusts are removed from the papules, there are discernible on the undersurface of the crusts horny plugs corresponding to dilated follicular openings Removal of the crusts causes bleeding Sebaceous material can be squeezed out of the follicles after the crusts are removed

Monilethrix. Monilethrix is a congenital and familial dystrophic condition in which the hair shows regular nodal constrictions at which it is likely to break off. Associated with the dystrophy is keratosis pilaris, a hyperkeratosis of the follicular stomas The hair is thinly distributed in the beginning After many hairs have broken off, the remaining hairs are set beside the short ones; both long and short hairs display variations in thickness and impart a shabby appearance to the scalp

Hereditary Xanthomatosis. Bloom and his co-workers recorded hereditary xanthomatosis as it occurred in 9 children of Syrian descent whose parents were second cousins The parents of these tainted siblings had no cutaneous or cardiovascular symptoms, although the father had hypercholesteremia. The mother had

8 half siblings, and 5 of them also had hypercholesteremia. This appears to support the hypothesis that hypercholesteremia rather than xanthoma tuberosum is the principal directly inherited factor and that this disturbance of lipid metabolism under certain conditions leads to cutaneous and cardiovascular changes. The hereditary cause of the disorder has been demonstrated but no adequate statistical data are available that warrant a final analysis of the genetic mechanism involved (see Lipidosis, Chapter 22).

Xanthomas are small, flat plaques of a yellow color in the skin. Microscopically the lesions reveal light cells with foamy protoplasm

Tuberous Sclerosis. Tuberous sclerosis is a rare heredofamilial disease in which there are multiple neurospongioblastomas in the brain The nodules and the accompanying sebaceous nodules of the skin have a moderately firm consistency, which is fancied to be that of a potato, hence the name tuberous Tumors often coexist in other organs, notably hypernephroma of the kidney and rhabdomyoma of the heart. The child is usually epileptic and mentally deficient.

The presence of sebaceous adenomas, small, closely set papular tumors of the skin, pink or brownish, appearing symmetrically on the face, chiefly about the nasolabial folds, bridge of the nose, forehead and chin, is the chief diagnostic feature The nodules sometimes are on the skin of the trunk and the intergluteal fold These cutaneous growths appear in adolescence, and therefore the condition may be difficult to recognize prior to this age The tubers may be situated within the cranial cavity and originate the localized or generalized symptoms of brain tumor

BACTERIAL INFECTIONS OF THE SKIN

Infections by the staphylococcus are the most common infections of the skin The staphylococcus produces furuncles, impetigo contagiosa, pyoderma, sycosis vulgaris and pyogenic paronychia The streptococcus too is a common cause of skin infections. It causes more serious infections of the skin than the staphylococcus, such as ecthyma, erysipelas and scarlet fever

Staphylococcal and Streptococcal Infections. *Acute staphylococcal dermatosis* is characterized by pustular follicular lesions. The appearance of the lesions varies with their depth The commonest form of the dermatosis is a superficial infection of the openings of the hair follicles These lesions are common and give little or no discomfort. Usually they are brushed away by bathing or by the clothing without one's knowing of their presence. Deeper infections of the follicles result in boils or furuncles

Furunculosis is more frequent in hot weather than at other times and may result from the rubbing of clothing, such as a collar, suspenders, belt or a cuff at the wrist; if there has been a previous lesion, pus from it may remain on the clothing, to be rubbed in somewhere else

A furuncle usually is caused by a staphylococcal infection in a hair follicle. The lesion begins singly about the neck, under the arm or in some other hairy portion of the body, and is first a central small pustule surrounded by inflammatory induration. Almost from the beginning the lesion is painful and tender The furuncle inspired the original classical description of an acute localized infection, namely, rubor, tumor, calor and dolor. Boils or furuncles destroy the follicles and on healing leave scars A furuncle is distinguished from a carbuncle by the fact that a furuncle has only one opening, whereas a carbuncle has multiple openings.

Metastatic infection in bones, kidneys and other distant points is not a rare complication of furunculosis; it occurs, however, in a relatively small proportion of cases. It is probable that pressure, squeezing, incision or other trauma to furuncles produces a transient bacteremia, which in turn results in metastatic abscesses (see the Fevers, Chapter 17).

Carbuncles often are caused by streptococcal infection. They are much larger than furuncles, are painful, and often cause fever and leukocytosis. Frequently they occur on the back of the neck and occasionally on the upper lip Owing to the peculiarities of the lymph drainage of the upper lip and the lower part of the nose, furuncles and carbuncles situated here are particularly dangerous because extension of the infection may enter the subdural spaces almost unhampered. Both furuncles and carbuncles may be the initial foci of infection which is spread by the blood stream to the heart, lungs, pleura, peritoneum, meninges and bones.

Hidrosadenitis is the term sometimes applied to axillary and inguinal affections by furuncles. The axillary lesions do not always suppurate and often are of the type called blind boils. The affection may extend to all of the axillary skin and subcutaneous tissues There may be difficulty in examining the area properly owing to the difficulty and pain caused in attempts to abduct the arm from the side

The prognosis in all the acute skin lesions caused by the staphylococcus, and in some infections due to the streptococcus, depends on understanding the normal progress of the lesions. The defensive cellular reactions initiated in the skin and subcutaneous tissues lead not only to the formation of pus but to an effective barrier or wall around the region of infection which prevents its extension. The collection of pus is shut in by this protective wall, occupies the center of the necrosed follicle, and forms the core of the boil. The lesion should be allowed to burst at its weakest point, or at most the weakest point lanced, and the contents and core allowed to evacuate spontaneously, a process which leaves a more or less aseptic cavity. Healing quickly ensues if the barrier has not been cut through by a knife or pierced deeply with a lancet At most, superficial lancing is all that should be permitted

Sycosis vulgaris is a chronic superficial folliculitis affecting mainly the beard. The infection may be most intractable It is maintained not by chronicity of the individual lesions but by their constant repetition The disorder may persist for years with little or no loss of hair, indicating that the hair roots have not been involved However, too much emphasis should not be placed on the superficiality of the lesion, for at times epilation of the hairs of infected follicles is not painful, indicating that the follicle is affected Owing to the chronicity of the infection, there are general redness and thickening of the affected region of the skin The presence of a chronic pustular inflammation of the hair follicles, limited to a hair-bearing area, especially the beard, is often sycosis vulgaris

The three common affections of the beard are impetigo, which clears quickly; tinea, more chronic, and sycosis vulgaris, which often lasts for years

Seborrheic sycosis, or sycosiform dermatitis, is not limited, like sycosis vulgaris, to the beard The beard of men and the eyebrows and eyelashes of both men and women may be affected Affections of the eyebrows and eyelashes are common. The infection begins after the age of puberty and produces painful swollen red eyelids and eyebrows The eyes matter and often are difficult to open on arising in the morning

On examination a chronic blepharitis with loss of eyelashes is present The blepharitis may appear after the dermatitis or may never be noticed There is a patchy dermatosis, a mixture of folliculitis with red, scaly dermatitis, spreading beyond the hair margin Similar patches occur on the upper lip, in the grooves of the lower lip and chin, and under the chin A distinct hypertrophy of the skin in the affected areas may be present. These patches are often persistent, lasting for years without a change in size

Granuloma pyogenicum is staphylococcal in origin. An injury has allowed the staphylococci to enter The lesions are on the fingers, at the nail fold They are small, red, shiny, pedunculated swellings composed of granulation tissue which bleeds easily

Streptococcal dermatitis is a superficial inflammation of the skin characterized by an acute onset of redness, thickening of the skin, and an abundant exudation of serum. In either the localized or the generalized forms of the disease the folds of the body, especially those behind the ears, and the scalp are more profoundly and frequently affected than other regions of the skin. As the inflammation subsides, there is formation of fine lamellar scales.

Erysipelas begins at one point on the skin of the face or neck and spreads rapidly, with a well-defined edge, from this point. The lesion is inflamed, hot, tense, shiny and painful. Secondarily occurring over this patch may be vesicles. If vesicles do not form, there is no subsequent scaling of the skin Erysipelas is always a serious disease Its prognosis is bad in the aged and the debilitated (see Chapter 17)

Impetigo contagiosa in some instances seems to be due to the streptococcus, and in others to the staphylococcus The vesicle, if cultured in the early stage, may yield streptococci or staphylococci It may be argued that the staphylococcus is either the primary or the secondary invader Children are most frequently affected, since infection is spread from clothing and contact Isolation of these patients should be mandatory

Superficial areas of the horny and the malpighian layers of the skin are the only parts involved. At first there are vesicles filled with clear fluid. The fluid becomes cloudy and the vesicle ruptures. Crusts form which are composed of dead epithelium, inspissated serum, leukocytes, fibrin and cocci. When these crusts are shed, the papillae are not exposed, and there is no bleeding. Healing is rapid and complete.

Examination reveals yellow crusts and vesicles situated mainly around the mouth, the cheeks, ears, and occasionally on other parts of the face. In the more severe infections the scalp and the fingers are involved. Often there are pinkish macules, indicating areas where the crusts have been shed from the face and scalp Pediculosis capitis may initiate the scalp infection and cause the spread and continuance of sporadic cases of the disease

When the fingers alone are affected, the lesions spread peripherally and for this reason may resemble a similar type of lesion on the face (*impetigo circinata*) which looks like ringworm. The reason for this resemblance is that healing of the bulla begins in and proceeds from the center. At the periphery the infection remains active, spreads and gives rise to a crusted, circular lesion which increases in size.

Impetigo neonatorum (pemphigus neonatorum) is a streptococcal infection which occurs in infants and is characterized by bullae about the mouth and fingernails The disease is not pemphigus

Impetigo is highly infectious. Not infrequently epidemics of the disease break out in lying-in hospitals The disease is often contracted by the mother On her the bullae appear about the breasts or places of contact All precautions are employed to prevent dissemination of the infection, such as thoroughly washing and sterilizing clothing, dishes, drinking cups, and feeding bottles All who attend these patients wash their hands thoroughly after the examination, before handling any objects

The diagnosis is based on the appearance on examination and on a recent occurrence of the disease in the institution or neighborhood The disorder is differentiated from chicken pox, pemphigus, dermatitis herpetiformis, dermatitis or eczema, and tinea circinata.

Impetigo barbae is a refractory form of impetigo which spreads rapidly and proves refractory to treatment This disorder is limited to the bearded regions and is characterized by the ease of epilation, followed by a drop of pus The disease is contracted in unsanitary barber shops

Infective intertriginous dermatitis or a similar disease may be caused by streptococci or other organisms The commonest sites of this disease are the folds behind the ears, with or without extension to the scalp Parts of the horny layer of the

skin are removed irregularly, leaving a raw area. The fold is thus rendered red and wet, while the scalp may be dry and scaly. Despite careful handling when the ear is moved forward to permit inspection of the fold, the thickened, swollen epidermis may crack and bleed. The disease is characteristically chronic and will return until all foci in the scalp have been eradicated

Acute infective dermatitis may result from various organisms. The lesions are asymmetric, superficial, well-defined, erythematous, vesicular, pustular, scaly patches. The margins of the lesion are undermined; the horny layer is raised as a scale with its free edge toward the center of the lesion It may not be possible to culture the causative organism.

Chronic dermatitis is common. There are three important conditions which occur in association with chronic dermatitis, namely, varicose veins; injuries to skin, nerves or blood vessels; and discharging wounds.

Varicose dermatitis is a common type of infective dermatitis In varicose dermatitis the inner surface of the lower third of the legs is affected As the disease progresses, ulceration develops which leads, when healed, if healing takes place, to the formation of rigid bound-down scars These scars may encircle the limbs by a hard fixed cuff of skin and subcutaneous tissue which further impedes the venous circulation

A dermatitis encir [illegible] sinus often occurs. The dermatitis is severe if [illegible] the sinus.

Dermatitis may fo [illegible] hands or other exposed parts, particularly if the injury has required long bandaging and dressing with salves The injury may be from any cause, but often there has been a puncture wound or injury to the underlying tissue as well as the skin A dermatitis which is difficult to heal may attend injury of a trunk of a peripheral nerve.

Infectious eczematoid dermatitis is distinguished by pustular and impetiginous lesions, perhaps due to the staphylococcus but more frequently to several and usually indeterminate organisms Inappropriate treatment often irritates this sort [illegible]

[illegible]

sodium hydroxide, for fungus will help to limit the etiologic possibilities Often the lesions will clear up if treatment other than cleanliness is discontinued

Acne conglobata is characterized by hypertrophy of the skin which accompanies the lesions of acne This hypertrophy is most noticeable about the nose, on the neck, back and buttocks These hypertrophic skin lesions of acne may become granulomatous and may form freely discharging sinuses, often deep and extensive. They may partially heal On each reactivation of the draining sinuses a generation of furuncles may occur These sinuses may resemble those of a tuberculous infection or one of the mycoses, such as sporotrichosis. In a patient of middle age a rapid increase in the area of induration around the sinus without other evidences for a [illegible]

[illegible]

These lesions may persist for weeks or months after perhaps a mild diphtheria

When a diphtheritic ulceration is suspected, smears and cultures from the lesions are taken at once, and if diphtheroid bacilli are found, antitoxin should be administered Virulence tests of the organisms may be made in order to arrive at a definite diagnosis

Tuberculosis. Tuberculosis of the skin is a serious but fortunately a rare disease Three women suffer from the disease for each man so affected. The disease is one of youth, before the age of 20 years It is acquired through contact, by an extension of an internal infection or by blood-borne infection

The tuberculous lesions on or about the nose and face are contracted by the direct spattering on the skin, from coughing or sneezing, of saliva or mucus which contains tubercle bacilli The postmortem wart occurring on the hands of pathologists is also an example of infection from contact. Butchers too may contract similar lesions from infected cattle

The skin over infected and caseating lymph nodes and around the sinus from tuberculous osteomyelitis may be infected.

Tuberculous septicemia may cause skin lesions over the body as a part of the miliary process. Miliary tuberculosis of the skin often appears suddenly during the course of pulmonary or bone tuberculosis and during convalescence from one of the exanthemas such as measles.

Tuberculosis of the skin, except for miliary tuberculosis, is a chronic disease The lesions progress by centrifugal spread. There are central healing and scarring while the periphery is active and slowly spreading The patient who has tuberculosis of the skin may die at an old age with the disease still active if there are no other active foci present in the body. When other active foci such as an active pulmonary tuberculosis or tuberculosis of the bone are present, the prognosis is that of the original infection The skin lesion may clear up and leave the other foci active.

For the purposes of description tuberculosis of the skin is usually divided into three forms, namely, (1) lupus vulgaris, (2) scrofuloderma and (3) miliary tuberculosis

Lupus vulgaris, or tuberculosis cutis luposa, is characterized by a great degree of chronicity It seems to be an inoculation type of tuberculosis which occurs on the head, face, nose, upper lip, cheeks, ears and neck of children from 4 years to 10 years of age The lesions are thus distributed because it is obtained from small droplets of tuberculous sputum disseminated in the air by coughing or sneezes of a tuberculous individual.

The process and the subsequent scarring may cause contracture of the mouth; destruction of the soft parts of the nose with necrosis of the cartilage, leaving a flat gaping orifice to the posterior nasal cavity; ectropion and, perhaps, blindness through corneal irritation and subsequent scarring, or loss of the auricles, by destruction of the soft parts and subsequent necrosis of cartilage

The usual lesion is a nodule from 2 to 5 mm in diameter It is raised, or it may lie on a level even with the surface In consistency it is softer than the surrounding skin, so that a blunt point drawn across the nodular area sinks as if crossing a hole in the skin In color the lesion is a light brown, clear and almost transparent The characteristics of the lesion are better observed if a glass slide is pressed firmly over it in order to expel the blood from the part The nodules often coalesce so that a larger area of affected skin appears which is actually one lesion There is a tendency to heal behind the spread of the lesion, and healing leaves irregular scars The mucous membranes frequently are involved.

Examinations of the lungs roentgenologically and of the urine and the sputum microscopically and by means of guinea pig inoculation for tubercle bacilli are important diagnostically A positive skin reaction to tuberculin seldom is helpful; if the reaction is negative, it rules out tuberculosis. The diagnosis depends on a skin biopsy However, in a young person the demonstration of the clear brown or reddish chronic nodules characteristically distributed on the face, nose and lips, accompanied with scarring and secondary epithelial changes leading to crusted warty forms, is usually sufficient for a diagnosis of lupus vulgaris. The prognosis is bad The disease persists throughout life.

Scrofuloderma (scrofula) is a direct infection of the skin from tuberculous lymph nodes of the neck or other underlying tuberculous infection. Draining sinuses develop and the adjacent skin is inflamed, swollen and cyanotic. Syphilis, for practical purposes, is ruled out if the serum reaction is negative

Miliary tuberculosis of the skin is but a part of the disseminated tuberculosis. It is a terminal manifestation of the disease elsewhere. Small papules appear which soften and ulcerate, and if life is prolonged the papules spread and coalesce and form ulcers. These lesions may occur about the mucous orifices without general distribution as a result of direct inoculation from infected discharges. The diagnosis is obvious.

SYPHILIS OF THE SKIN

n important cause of skin disease. In tropical ne cause of much suffering

lesions of syphilis become manifest during the first year after birth The important lesions of congenital syphilis are enumerated as (1) interstitial keratitis, (2) Hutchinson's teeth and (3) labyrinthine disease (see Diseases of the Lens, Chapter 4)

The skin lesions consist of a wrinkled, loose-appearing skin which has been described as old-mannish in appearance A pemphigoid or papular eruption may be present on the palms and soles and over the legs. The bullae of the pemphigoid eruption are of longer duration than those of impetigo neonatorum The papular lesions are commoner in the anal and the genital regions than on other parts of the body These papules may be erythematous in appearance and may closely resemble those of acquired syphilis

Often neither parent of a congenitally syphilitic child will admit knowledge of a syphilitic infection The physician is in turn interrogated concerning two possible sources of the child's infection. (1) Could it have come from the child's grandparents? (2) Could syphilis have been accidentally acquired? The answers are: (1) Congenital syphilis is from the mother to the child (2) Accidental infection occurs, but usually syphilis is acquired as are all venereal infections, and that is by direct contact, which is usually through sexual intercourse. However, accidental inoculation may occur through a breach in the skin or in a mucous membrane by such means as infected vessels for eating and drinking, infected instruments, especially the tattoo needle, kissing infected persons, droplet infection, of a physician's eye during examination of a syphilitic throat, or direct infection of a finger during the examination of a patient In some instances an admission of these means of acquiring syphilis may save much time for the physician. However, in reality the physician should realize that it may not be too important how syphilis was acquired if the patient has it.

skin is thickened and inelastic.

Acquired Syphilis. The *primary lesion* (hard chancre) appears from 2 to 6 weeks after infection If no ulceration has occurred, there is a hard, raised, red papule, the surface of which is glazed, moist, and bleeds on being traumatized If the primary sore is on the external genitalia, the patient always ascribes it to

manent after ulceration The regional lymph nodes are enlarged early The primary lesion may be small, may last only a week or two, and is described as just a pinpoint sore

The diagnosis is confirmed by the presence of the treponema in serum from the lesion on examination under darkfield illumination Positive results of serologic tests are not present for several weeks.

Extragenital chancres occur around the fingernails, the face, lips, cheeks, mouth, breasts, abdomen, and in fresh tattoo injuries of the skin.

The *secondary lesions* of syphilis are general surface lesions and skin eruptions In many instances the skin lesions of syphilis may be precisely described as macular, papular and nodular syphilides.

Symptoms referable to the body as a whole, or general symptoms, vary in degree and are not predictable There are often a feeling of ineptitude, pains through the body affecting the arms and legs, and headache which occurs at night after the patient has retired to bed There may be a low-grade fever during the evening hours In an occasional instance there are high fever and skin eruption which spreads rapidly, causing a serious disability. This is the so-called malignant syphilis. These rapidly developing secondary lesions of syphilis occur over the body and involve the mucous membranes as well Involvement of the mucous membrane by syphilis may be severe, with ulceration and deep sloughing of the tonsils and nasopharynx

A syphilitic eruption usually commences as a macular erythematous eruption over the abdomen, trunk and face The eruption of syphilis is commonly present on the palms of the hands and on the soles of the feet In the beginning it is truly a macular eruption. There is no itching The eruption varies in color and intensity and may simulate that of measles and of influenza. The color of a syphilitic eruption has often been described as coppery or fawn The lesions are in, not on, the skin

The *macular syphilid* is a common macular lesion that occurs on the body This lesion often commences around the umbilicus and from this part spreads over the thorax and the flexor surfaces of the extremities; it occasionally extends to the neck, but rarely to the face. The average diameter of the lesions is about 1 cm The edges are ill defined The lesions are at first a light yellow, which changes to a reddish color. There is no itching, and no scaling Usually there are other symptoms of syphilis present, such as the scar of the initial lesion or chancre. There also usually are enlarged lymph nodes in the posterior triangle of the neck and in the axillary, epitrochlear and inguinal regions. Alopecia may be present Sore throat and general aches and pains may be present, and in women there may be a history of miscarriage

There are two forms of *papular syphilid* One form, the small papular variety, usually occurs over the flexor surfaces of the extremities As a rule, the lesions are grouped. The papules are small and discrete, may be slightly scaly, and sometimes are associated with pustules On palpation the lesions can be felt situated in the corium The second form, the large papular variety, may occur on the face, neck and genitals as flat papules, often clearing up in the center, thus sometimes being designated as an annular type of syphilid These lesions are sometimes scaly, almost always accompanied by induration, and usually by other symptoms of syphilis

The *nodular syphilides* in syphilis are late secondary or tertiary lesions. These nodules may begin as millimeter-sized papules which are well defined Frequently they are multiple, two or more in number. The individual syphilid is firm and smooth, and reddish in color. As the disease advances, the nodules increase in size, ulcerate, and have the so-called punched-out appearance that is characteristic of syphilitic ulcers. These lesions often accompany other symptoms of syphilis. They are painless.

During the secondary stage of syphilis the serologic reactions are positive

A large papular eruption of syphilitic skin lesions may closely simulate lichen planus Lichen planus is itchy and occurs on the palmar surfaces of the wrists, the inner aspects of the knees, and the legs below the knees.

Both psoriatic lesions and syphilitic lesions may be circinate. Psoriasis is a disease of long-standing and recurrent manifestations, whereas syphilis is a disease of recent manifestations and rapidly spreading lesions and involves the true skin.

Leukoderma frequently occurs about the region of the neck and is accompanied

with pigmentation around the characteristic small white areas. Stubborn patches of pinta and syphilis about the face and neck, often lasting for years, simulate the lesions of chronic psoriasis or tuberculosis A unilateral psoriatic-appearing lesion on the buttock, calf or sole should be regarded with suspicion. The ringed and horseshoe manifestations of syphilis may resemble psoriasis or ringworm, but neither of these diseases affects the true skin.

The serologic tests for syphilis are now most reliable and diagnostically dependable. However, there is a possibility of false positive serologic reactions. In all questionable instances of these reactions a decision about validity of the test usually can be made from the history and the findings. All false positive and serologic fast-reactions should be checked by examination of the cerebrospinal fluid.

INFECTIONS OF THE SKIN DUE TO VIRUSES

Eczema Herpeticum. Kaposi's varicelliform eruption and Juliusberg's pustulosis vacciniformis acuta are synonymous names for eczema herpeticum.

Eczema herpeticum is due to the herpes simplex virus and occurs in children who, as a rule, already have an eczema. In the majority of cases, according to Barton and Brunsting, this eczema is a primary herpetic infection and as such is accompanied by a severe systemic illness which occasionally is fatal. A less severe form of the disease is observed in those who have circulating antibodies in the blood In these patients there is often a history of contact with a manifest infection by herpes simplex

The close association with atopic eczema may implicate the virus-potentiating activity of histamine, or the wide expanse of denuded skin so common in these patients may merely provide a good nidus for exogenous infection with the virus The disease may resemble eczema vaccinatum

The vesicles develop rapidly, in large numbers and in successive generations, for 3 or 4 days to a week The largest number of the varicella-like vesicles occur on the already eczematous skin A small number of grouped lesions appear on the intact skin. Those which appear first undergo desiccation, rupture, and expose the corium or they become encrusted and shed The outcome in the majority of cases is favorable

The diagnosis can only be suspected clinically and is established with certainty by demonstration of the virus by viral technics

Varicella-Herpes Viruses. The similarities of varicella and herpes zoster lie in the nature of their viral agent (*Briareus varicellae*), their vesicular eruptions, and their intranuclear inclusion bodies, while their greatest differences are found in age incidence, epidemiology and changes in the central nervous system; hence their widely different symptomatology (see Viral Infections, Chapter 17)

Varicella, or chickenpox, sometimes also called herpes zoster, zona, shingles or zoster, is a mild communicable disease caused by a virus similar to that which induces herpes zoster *Herpes zoster* is an affection limited to the cutaneous distribution of a cutaneous nerve

Varicella (*Ch*[illegible]) Th[illegible] [illegible]eks
In 24 hours after [illegible] or
accompanied with [illegible] and
trunk, spreading in some cases to the mouth and pharynx and extremities. In chickenpox the lesions are usually most abundant over the trunk, as contrasted with the face and extremities in smallpox The eruption occurs simultaneously with the fever, and its duration is proportional to the height and persistence of the fever.
[illegible]

Vesicles on the laryngeal mucosa, about the eyes and genitalia and in the hair may become infected secondarily and cause much discomfort.

On occasion an encephalitis, symptomatically similar to that accompanying herpes zoster and measles, complicates chickenpox. Patients usually recover from chickenpox encephalitis

Verrucae (Warts). Warts are small, benign papillary overgrowths, which vary in size, color and shape They occur slightly more commonly in women than in men. Certain families seem to have a relatively greater susceptibility to infection than other families. Warts are auto-inoculable and transmissible and may disappear without treatment There are four distinct types according to Lane. verruca vulgaris, verruca plana juvenilis, verruca plantaris and verruca acuminata.

The abnormal cellular hypertrophy is due to a local infection with a virus. Whether separate viruses cause the four different forms of verruca or whether the different forms are clinical variations resulting from one virus is unknown Rudloff expressed the belief that venereal vegetations and verruca vulgaris are sister growths due to the same filtrable virus, which manifests itself by papilloma formation on mucous membranes or on thin skin and by wart formation elsewhere.

Verruca vulgaris is the commonest type. These warts occur predominantly in children and adolescents and appear most often on the exposed areas, particularly on the hands and fingers, but any portion of the skin surface may be involved Variants of this type are the threadlike filiform wart of the eyelids and face and the digitate warts which project from the scalp, face and neck.

The lesion of verruca vulgaris is a raised, circumscribed, solid, round, gray or yellowish gray papule varying in size from 2 to 10 mm. The surface at first is flat and smooth but may become scaly, crusted, or fissured The warts may be single or multiple; frequently there is a primary mother wart, which in time is joined by satellite lesions

Verrucae planae juveniles, known as flat warts, are slightly raised, small, flesh-colored, round or angular papular lesions which are distributed over the face, neck, hands and wrists Almost universally multiple, these lesions occur most often in children and young women They may resemble vesicles or may closely resemble the papules of lichen planus and, rarely, those of molluscum contagiosum. They produce a dirty appearance on the face when they have coalesced and are situated on the chin

Verrucae of the plantar type occur on the padded areas of the soles and heels, less frequently the sides of the feet, the under surfaces of the toes, the palms and palmar surfaces of the fingers There may be a single wart, but often there are small satellites in the vicinity of the original lesion Differentiation from a callus and a clavus may be difficult but is facilitated by paring the surface of the verruca A wart is revealed as a well-defined, discrete, gray, round or oval area often containing small dark specks or threadlike lines, which are deposits of blood pigment If the surface of a callus or corn is pared, a smooth, hard, yellow growth containing no blood stains is seen

A variant of the plantar wart is the so-called *mosaic wart,* which has been well described by Montgomery and Montgomery as a warty patch, horny and granular with an irregular border, and varying in width from 1 to 10 cm Comparatively painless, the patch is situated under the pressure points and may extent onto the toes and behind the heels. It is often mistaken for callus. Paring reveals the intracellular nature of the patch, which consists of many small individual cores so closely grouped that they resemble a mosaic pattern The pain and tenderness of plantar warts may be sufficient to hamper the activities of the patient seriously.

Verruca acuminata, known also as condyloma acuminata and venereal wart, occurs chiefly on or about the genitalia and the anus, in the axillae and groins and on the navel. As single or multiple, discrete or confluent, raised, filiform or

papillomatous lesions, whose surfaces are often moist and macerated from the secretions of the surrounding organs, they are attached by broad or narrow bases. Verrucae acuminatae may be sensitive, painful and malodorous and may interfere with function

Warts may be difficult to treat successfully Many patients are convinced of the therapeutic virtues of witchcraft for the cure of warts.

INFECTIONS OF THE SKIN DUE TO HIGHER PLANT ORGANISMS
(*The Superficial Mycoses*)

Fungi, microscopic members of the plant kingdom, belong to phylum Thallophyta, orders Algae and Fungaceae. The order Fungaceae comprises bacteria (Schizomycetes), true fungi (Eumycetes) and slime molds (Myxomycetes). The Myxomycetes are nonpathogenic Of the four subclasses of true fungi the Hyphomycetes (Fungi imperfecti) contain the common pathogenic fungi present in lesions of the skin and hair. A skin fungus which does not invade the hair follicle is termed *Epidermophyton* Sabauraud called the fungi which proliferate on the surface of the hair Microspora: the two groups (Trichophyta) which invade the hairs are endothrix and ectothrix, depending on the situation of the spores in relation to the shaft of the hair.

Ringworm. Ringworm infection of the skin according to Lewis and Hopper is arbitrarily divided into regional varieties, namely, scalp (tinea capitis), beard (tinea barbae), smooth or glabrous skin (tinea glabrosa), folds of skin (tinea cruris) and feet and nails (dermatophytosis and onychomycosis)

Tinea Capitis (*Ringworm of the Scalp*). Tinea of the scalp usually is due to one of two Microspora, *Microsporum audouini* and *Microsporum lanosum*

However, both the *Trichophyton* and the *Microsporum* group have (1) species which are pathogenic principally for certain lower animals (zoophilic) and (2) species which are pathogenic principally for human beings (anthropophilic).

Infections contracted from animals have two important characteristics; they are but slightly, if at all, contagious among human beings, and they either are self-limited or respond to topical therapy. Humans are poor hosts for this group of fungi, and, as Lewis and Hopper showed, the self-limited features of these fungi may be accounted for by the development of antibodies and the production of an inflammatory reaction in the neighborhood of the infected hairs

In the United States, *Microsporum lanosum* is the important animal (zoophilic) representative of the Microsporum group and is generally transmitted by cats or dogs Unlike the disease contracted from cattle, *Microsporum lanosum* usually produces but slight inflammatory reaction. Several members of a family may be infected from the same pet, but extensive epidemics do not occur. Infections produced by *Microsporum lanosum* must be differentiated from the epidemic form (*Microsporum audouini*) because they are self-limited and nonepidemic.

Infections with human (anthropophilic) fungi are contagious and are usually resistant to topical therapy The lack of antibodies and severe inflammatory reaction is ideal for survival of the fungus and allows infection to persist for years.

Microsporum audouini has been responsible for the recent rapid increase in ringworm of the scalp in the United States

Microsporum audouini may cause epidemics in institutional children When the condition is first discovered, there are several small areas in the occipital and temporal regions in which the hair is dull and broken off The surface of the patch is usually scaly Occasionally a considerable degree of inflammation may be present but this is not the rule The lesions spread peripherally, finally reaching 1⅕ inches (3 cm) or

more in diameter. There is little tendency for the infection to spread to other parts of the body.

Trichophyton violaceum develops insidiously and is widely dispersed over the scalp It invades the cortex of the hair, causing the hair to break off close to the scalp or just below the surface of the scalp which gives the appearance of an ingrowing hair. The disease may heal at puberty.

Microsporum lanosum causes a fungous infection of the scalp of children and occasionally involves glabrous skin. It may be, at times, contracted from pets (kittens). The initial lesion is frequently the largest There is loss and breaking off of hair in the affected patches with marked inflammation and *tenderness The duration of the disease* is only a few months

Microsporum fulvum resembles *Microsporum lanosum* except there is a tendency for the inflammation to remain localized to only one part of the scalp

Endothrix *Trichophyton causes favus Favus usually is a follicular involvement of* the hairs but it may occur with minimal follicular involvement. The disorder may spread to the nails or to the glabrous skin

On the scalp favus begins as a small area of scaly inflammation in which the hair follicles become festered Breaking of these small pus pockets results in yellow crusts which increase in size and finally become cup-shaped (scutula) The scutula are yellow, friable scabs pierced with hair. There is intense itching and a moldy odor like that of rats The hair of the scutula falls out The skin becomes atrophic and due to the spread of the disease an irregular permanent baldness ensues. Spontaneous recovery from the disease eventually occurs However, when there is a minimal follicular involvement, there is only a diffuse superficial but adherent scaling of the scalp, with little, if any, permanent alopecia.

Trichophyton gypseum is often contracted from pets and farm animals It may vary in intensity and distribution of its manifestation in accordance with susceptibility to it Widespread infections involving the hands, feet and face are due to increased susceptibility or increase in the virulence of the infective agent The characteristic lesion is a severe inflammatory reaction of the scalp and the development of kerion.

In many instances bacterial infections of the skin and fungous infections are both present This is particularly true of an infection like *Trichophyton crateriformi* When a mixed infection is present part of the manifestations—the crusting, kerion and shedding of hair—is caused by the secondary infection by bacteria and other fungi The treatment of the bacterial infection often suffices to effect a recovery.

In summary the manifestations of tinea of the scalp are partial loss of hair in *patches, breaking off and lack of luster of the infected hair, and varying degrees* of inflammation Atrophy and scarring may follow certain types of infection Kerion formation is common In appearance a kerion is a marked tissue reaction to the infecting microorganism, one of several species of fungi The pustular lesion is a painful, elevated, boggy, erythematous, localized tumefaction with simple scaling at the bottom.

DIAGNOSIS. The diagnosis of ringworm of the scalp may be made reasonably accurately by microscopic study of scrapings from the lesions, skin or hairs when properly prepared.

Patients who have ringworm of the scalp vary in their reaction to trichophytin, mainly in accordance with the type of infecting microorganism and with their own powers of resistance *There is usually more response when the fungus is also* pathogenic to animals.

A scalp infected with ringworm will show, under filtered ultraviolet rays, a characteristic fluorescent effect whenever infected hair is present. The ultraviolet rays are diagnostically important in revealing the presence and extent of *the ring*-worm infection of the scalp.

Tinea Barbae (*Ringworm Infection of the Beard*) Infections of the beard commonly are due to *Trichophyton gypseum* There are occasional instances of infections caused by *Microsporum lanosum, Trichophyton rosaceum, Trichophyton violaceum* and *Trichophyton purpureum.* The spread of these infections is thought

to occur in the barber's shop. Animals are known to be carriers of *Trichophyton gypseum* or *Microsporum lanosum* The disease may be contracted by contact with those who have infections of the scalp or of the glabrous skin. There are two types of infection, (1) diffuse inflammatory and (2) sycosis.

The diffuse inflammatory process is contracted from pet animals. The beard in the affected areas loosens and epilation is easy In the sycosis type of tinea barbae, once the infection is established, it slowly spreads as a mild crusted folliculitis with breaking off of the invaded hair (*Trichophyton violaceum*) or similarly without the formation of hair stumps (*Trichophyton purpureum*).

The diagnostic value of the reaction to trichophytin depends on the type of infecting organism. *Trichophyton gypseum* and *Microsporum lanosum* infections give definite positive reactions to skin tests In the other infections the skin reactions are irregular and cannot be depended on as tests of diagnostic value.

If the shaft of the hair has been invaded, a fluorescence of the infected hair is observed under filtered ultraviolet radiation. Endothrix organisms give the fluorescence. The ectothrix organisms produce no fluorescence under the filtered ultraviolet radiation The inflammatory type of tinea barbae has to be differentiated from sycosis barbae, iododerma or bromoderma, and syphilis.

Tinea Glabrosa (*Ringworm of the Smooth Skin*).—Fungous infections of the glabrous skin occur as scaly circinate patches, as solid plaques, or in geographic configurations

Microsporum lanosum (*M. canis*) obtained from contact with kittens or other pets or from an infected individual is the usual cause of ringworm of the smooth skin. Less commonly infection of the smooth skin extends or is carried from scalp infections (endothrix *Trichophyton*) or from feet infections (*Trichophyton gypseum, Trichophyton purpureum*)

Microsporum lanosum infection is manifested by an erythematous ringed lesion which may gradually increase to a diameter of 5 or 6 inches There are usually minute vesicles along the border, the surface is scaly, and the center appears unaffected Sometimes two or more concentric rings may appear in a single lesion. The lesions are commonly present on the faces or necks of children with tinea capitis The backs of the hands and other exposed parts are the usual sites of the first lesions in patients who catch the infection from an outside source. New lesions may develop on various parts of the skin, depending on extension and on transfer of the organisms from the original focus. The subjective symptoms are usually mild, although the infection is itchy and subsequent scratching may contribute to its spread

The eczematous type of smooth skin infection by tinea may simulate in appearance almost any form of dermatitis The primary eczematous type is the initial response to infection (usually *Trichophyton gypseum*) In this form of eczematous dermatitis the first lesion (or lesions) is the vesicle, and vesicles continue to form, rupture and become crusted The infection spreads peripherally, there being no tendency to central clearing The lesions remain ill defined or become circinate, with active vesiculation along the periphery.

The secondary type of eczematous dermatitis from tinea is caused by medicaments or by treatment producing primary irritation, which transforms the circinate lesions into vesicular, oozing patches surrounded by varying degrees of dermatitis.

Trichophyton purpureum may cause a large surface eruption of skin of the trunk The infection begins at one or more points and migrates in a thin line over an ever-widening area. The affected skin is dull red and presents a slight infiltration and scaling on the surface As the border of the lesion advances, behind it the skin is lighter owing to loss of color. Persistent itching is a constant symptom.

The diagnosis is usually established by cultural methods from the skin lesions.

Fungi are absent in material taken from the lesions. The trichophytin reaction is usually negative in cases of uncomplicated tinea of the glabrous skin

The prognosis varies with the infecting microorganism Ordinary tinea circinata usually responds to treatment within a week or two The eczematous type takes longer to respond, endothrix *Trichophyton* infections still longer, and the infections due to *Trichophyton purpureum* are resistant.

Tinea Cruris (*Dhobie Itch*). Tinea cruris is a superficial fungous infection (caused chiefly by *Epidermophyton floccosum* and species of *Trichophyton*) confined usually to the medial surface of the proximal third of the thighs, although other parts of the skin may become affected. The infection may be obtained from contact or from infected articles of clothing Another form of the disease is a contact dermatitis of various causes, in India it has been attributed to the marking fluid, bhilawanol oil (from *Semecarpus anacardium*, of the family Anacardiaceae), used on laundry by the native washermen (dhobie). Tinea cruris at times may assume epidemic heights.

The eruption is usually bilateral and symmetric, it favors the upper inner portions of the thighs but may extend up to the pubis and as far back as the sacrum The axillae, the umbilicus, the inframammary areas and the interdigital webs of the feet are occasional sites of the infection. Vesicopustules are sometimes seen on the soles. The friction of clothing during hot weather causes varying degrees of secondary eczematization

The area of the rash is well marginated by a border of minute vesicopustules The surface is scaly and there is little or no tendency to central clearing The lesions are brownish red.

The absence of evidence of tinea infection of nails, hair, feet or smooth skin elsewhere over the body limits the likelihood of other tinea infection.

Tinea cruris usually does not initiate sensitization to trichophytin A test with trichophytin usually elicits a negative or a mildly positive reaction. With *Trichophyton gypseum* a positive reaction is usual, but when *Trichophyton purpureum* is the causative fungus, a negative reaction is common.

The ordinary form of the disease usually responds readily to medicinal applications but tends to relapse. The lesions caused by *Trichophyton gypseum* are likewise readily cured, but those due to *Trichophyton purpureum* are extremely obstinate.

Dermatophytosis. The term dermatophytosis refers to a superficial fungous infection of the skin The disease (sometimes called athlete's foot) is usually acquired by transfer from organisms affecting the hands, feet or nails.

Dermatophytosis is a common disease It is commonest in boys and men from 15 to 25 years of age Hyperhidrosis is commonly present in those who have dermatophytosis

Some lesions of the feet and nails resemble dermatophytosis of fungous origin but may be due to causes other than fungous infections. If the dermatophytosis is due to a fungus, *Trichophyton gypseum* and *Trichophyton purpureum* can be cultured from the lesions *Microsporum albicans* and *Microsporum lanosum* may occasionally be present

There is an acute inflammatory type of the disease due to *Trichophyton gypseum*, and a chronic type, due to *Trichophyton purpureum*.

The inflammatory type (*Trichophyton gypseum*) commences on the feet and is manifested by vesicles between the toes or on the soles. The skin between the fourth and the fifth toes is very commonly affected The vesicles, or bullae, rupture and the skin at the site of the lesion becomes macerated, soggy and white. This appearance may be maintained for weeks, months or years On peeling away of the soggy white debris of skin, fissuring and cracking and erythema occur

During the hot weather there may occur a pruritus of the toes, some swelling, and the appearance of vesicles on the soles and perhaps on the sides of the toes and

feet. Synchronously with the evidence of local inflammation on the feet, vesicles may appear on the palms of the hands and sides of the fingers. These eruptions are due to the dissemination of products of fungi through the blood stream, and the lesions are known as dermatophytids. They are sterile on culture.

In instances in which there is an increased sensitivity the eruption may spread to involve the intertriginous areas and folds of the upper parts of the thighs, the *perianal region, the axillae, the inframammary regions and the umbilicus* A secondary infection of the involved areas by pyogenic organisms is common. This secondary infection may overshadow the characteristics of the fungous disease and appear as an eczematoid dermatitis

Infection of a nail with *Trichophyton gypseum* may be superficial, causing only a white patch on the surface or in the substance of the affected nail (leukonychia trichophytica). A more severe infection causes the nail to turn pale yellow, opaque, lusterless and friable, and separation of the nail may occur Subungual hyperkeratosis and uneven dystrophic changes in the nail are frequent, but paronychia is rare Mild to severe pain may occur

The appearance of the eruption (with itching) on the feet and on the hands is peculiar to *Trichophyton purpureum* infections. Lesions of the feet and hands may occur on the soles and palms, the sides, the dorsa, the toes and fingers or the nails

Of patients who have *Trichophyton gypseum* infections, about 7 of every 10 give positive reactions to skin tests with trichophytin in 48 hours, of those who have *Trichophyton purpureum* infections about 3 of each 10 give positive reactions after 48 hours Reactions to the trichophytin skin test in those who have dermaphytosis from other organisms are so irregularly present that the value of the test for purposes of diagnosis is doubtful

The diagnosis is made by culture and identification of the offending organism. In most cases of inflammatory tinea the reaction to the trichophytin test is positive. When *Trichophyton gypseum* is the causative fungus, the prognosis is hopeful If *Trichophyton purpureum* is the offending microorganism, cure is difficult The duration of the infection and the extent of involvement of the skin are often determinative factors in the prognosis.

Tinea Versicolor (*Pityriasis Versicolor, Chromophytosis*). The microorganism, a species of fungus, that causes tinea versicolor is known as *Malassezia furfur*. The disease affects adults of both sexes. The lack of personal hygiene sometimes seems to be a predisposing cause in many instances of the disease

The disease manifests itself by light yellow-colored scaly macules and patches starting from barely visible lesions in single or multiple foci. The sites of predilection are the thorax, the abdomen and the back At times the eruption favors intertriginous locations but it may involve large stretches of skin.

During the summer or autumn a patient who has tinea versicolor may exhibit apparently depigmented areas on the surfaces of the affected skin which are exposed to sunlight The patches occupy the sites of lesions of tinea versicolor. Their color is not the pale white, with demarcated edges and with increase of pigment at the periphery, as is present in vitiligo The condition appears year after year, and despite becoming less noticeable during the winter it will reappear during the summer

The lesions of tinea versicolor under filtered ultraviolet rays reveal a fluorescence Examination for fungi, combined with observation of the patient under filtered ultraviolet radiation, is diagnostic The ordinary form of tinea versicolor is not confused with any other disease

Erythrasma. Erythrasma is a superficial mycosis resembling tinea versicolor The causative fungus is *Actinomyces minutissimus* (*Microsporum minutissimum*). The means of transmission of the infection is unknown. The disease is less common

than tinea versicolor. Erythrasma is commoner in young men, whereas tinea is commoner in old men, and the lesions of erythrasma are limited to one or more in number, situated in the axillae, the groins, the intergluteal cleft or other intertriginous areas. The lesion commences as a small, scaly, well-circumscribed macule with a reddened border which gradually enlarges to form variously sized patches. The color varies through mixtures of red and brown, the exact shade depending on the amount of pigment in the skin, the age of the lesion (the older the darker) and the amount of sunlight to which the lesion has been subjected.

In all cases a mycologic diagnosis should be made by identification of the organism. The demonstration of the microorganism may be difficult

Otomycosis (*Myringomycosis*). Otomycosis affects the external ear and the aural canal. This condition may be due either to fungi or to streptococci. No age is exempt, although the majority of patients are young adults

The external ear around the meatus is swollen and red. A moist mass of debris fills the canal When this is removed, the affected skin is seen to be exudative. The disorder may extend down the canal and affect the drum.

Lepothrix (*Trichomycosis Axillaris*). Trichomycosis axillaris (*Actinomyces tenuis*) is characterized by nodes on the axillary hair, often with the formation of red or black pigment. Micrococci are said by some to be responsible for the formation of this pigment and not *Actinomyces tenuis*

Irregular concretions form in the axillae and attach themselves to the hair The attachment is firm, and the nodes (concretions) are difficult to dislodge The entire circumference of the hair is involved. The concretions are usually yellowish, red and black varieties are uncommon The concretions exhibit fluorescence under filtered ultraviolet rays.

Tinea Nodosa (*Piedra*) This disease, caused by *Trichosporon giganteum,* is manifested by small, hard nodes along the involved hair shaft The disease is confined to scalp hair of women in South America The European and Asiatic *varieties affect only the male beard and mustache, never the scalp.* The nodules of both varieties are stony hard and light or dark brown. From 1 to 25 nodes may be present on one hair. Shaving is a certain cure

Chromoblastomycosis (*Dermatitis Verrucosa*) Three fungi, *Hormodendrum pedrosoi, Hormodendrum compactum* and *Phialophora verrucosa* are recognized as causing verrucous nodules. The tissue reaction consists of granulomatous changes similar to those resulting from the presence of a foreign body, a tuberculoid reaction and miliary abscess formation.

The lesions are situated on the leg Each lesion commences as a verrucous nodule or an ulcer The nodule may be reddish, purplish or brownish. After many months or years verrucous masses are formed by coalescence of two or more lesions and their subsequent growth Growth continues until large pedunculated, fimbriated, cauliflower-like masses are formed Infection by bacteria causes a foul discharge and edema of the food and ankle. The lesions resemble psoriasis, lupus erythematosus and tuberculosis

Mycologic study and the results of inoculation of guinea pigs may reveal distinguishing features of this disease

Moniliasis. The causative microorganism of moniliasis is *Candida albicans* The organism is etiologically weak It does not occur on the normal skin. It is a common inhabitant of the orifices of the body and the gastrointestinal tract Once *Candida albicans* is established, it may cause either superficial or deep mycotic infections. *Only the skin infections will be considered here*

Housewives, bartenders, waiters and bakers appear to be more susceptible than other persons to the infection because of their occupational sweating and often-wetted hands When moniliasis (*Candida albicans*) infections are limited to a localized area of skin, they are termed the moniliid type

These localized affections of the *skin* are manifested by well-defined, bright red, exuding patches with scalloped borders occurring mainly in intertriginous areas. Bordering the zone of intertrigo, small flaccid vesicopustules may be present. A monilial intertrigo occurs in the axillae, the groins and the intergluteal fold The process may extend from a primarily intertriginous location to the flat skin, and large surfaces of skin of a susceptible person may be affected.

Candida albicans infections at the angles of the mouth may occur as rhagades or perlèche, the bases of which are bright red This type of perlèche cannot be easily distinguished from those types due to vitamin deficiency secondarily infected by streptococci.

Onychia and paronychia of the *fingernails* and occasionally of the *toenails* occur. Infection of multiple digits is the rule. Rarely is only one digit involved. As a rule, the paronychial tissues are the first to be affected A thin purulent discharge may appear under the nail fold Transverse ridges appear on the nail, though it remains hard. The nail gradually becomes thickened and distorted at the edges and may become yellow The natural glazed surface is unaffected. The edges of the nail may be eroded. There is no pain except by pressure on the nail and from the paronychia when dry

Thrush is a manifestation of *Candida albicans* It is most commonly seen in infants It may have been contracted at the time of birth from a *Candida albicans* vaginitis of the mother. A whitish, loosely adherent membrane is attached to the inner surface of the cheeks or to the palate and sometimes to other portions of the oral mucosa. The whitish membrane resembles the curd of milk and is distinguishable by the fact that it can be wiped away without leaving residual surface markings.

The presence of *Candida albicans* in the *vagina* usually does not indicate the presence of a *Candida albicans* vaginitis In women sufficiently susceptible the organism may produce pruritus and vaginitis accompanied with a thin vaginal discharge. It is even less likely that *Candida albicans* is of etiologic importance in *pruritus ani*

Moniliid lesions may occur as sterile vesicular lesions on the *hands* and localized or widespread erythematous vesicular exudative patches caused by dissemination through the blood stream of products of *Candida albicans*.

The diagnosis is difficult, for culturing of *Candida albicans* from a lesion does not identify the lesion as being caused by *Candida albicans* The disease no doubt occurs, but to make the diagnosis is a dangerous practice except when the lesions are around the nails of the hands Identical lesions about the nails may be caused by bacteria. The oidiomycin test is of no value in differential diagnosis. When infection is generalized, the outcome is often fatal (see Deep Mycotic Infections, Chapter 17).

CYSTS, SINUSES AND FISTULAS

Cysts, sinuses and fistulas are of common association with the cutaneous structures The commonest cysts are the epidermal cysts.

Anderson classified cysts, sinuses and fistulas as they are here described

Epidermal Cysts. Epidermal cysts have an epidermal lining but lack definite dermal structures Epidermal cysts are generally found in the cutis or corium and are only rarely situated below the cutis in the subcutaneous tissue. Occasionally, such cysts may be attached to the epidermis by a band of epithelial composition. The great majority, however, are not connected with either the overlying epidermis or any cutaneous gland or structure.

Degenerative changes occur with considerable frequency in epidermal cysts. Rupture of the epithelial capsule is common, and a foreign body giant cell inflammatory reaction ensues Fibrosis and relative involution may occur and, while calcification is frequent, true ossification is rare. Malignant degeneration may occur (*epithelioma*).

Sebaceous Cysts. Sebaceous cysts result from the occlusion of sebaceous glands, and hence their epithelial lining is composed of secreting sebaceous gland cells. The contents of the true sebaceous cyst are light yellow in color, homogeneous in consistency, and have a disagreeable, distinctive odor.

The multiple cysts occurring on the trunk in association with acne and seborrhea are true sebaceous cysts

Sweat Duct Cysts. Sweat duct cysts are associated with the sweat ducts and sweat glands and are generally termed hydrocystomas or sudoriparous cysts These cysts appear on the cheeks as solitary shiny, translucent and fairly deep lesions 1 mm in diameter Occasionally, larger ones occur on the upper eyelid The larger solitary lesions are best removed surgically, the smaller lesions can be destroyed by electrodesiccation.

Dermoid Cysts. True dermoid cysts are congenital in origin and are situated in areas where there was a connection with embryologic fissures and clefts They occur in the cutis or the corium. They may occur at either the inner or the outer canthus of the eye in relation to the bony walls of the orbit, or on the midline of the nose along the lines of closure of the nasal bones, or along the anterior midline of the neck

The history of a *dermoid cyst of the neck* is that of a midline swelling in the neck above the thyroid gland which has been present for years Either because of an increase in size or for cosmetic reasons the patient consults a physician. The diagnosis of a cyst or a mole is made and there is an attempt to treat the lesion either by electrodesiccation or by surgical removal A few hairs are generally removed at such times. There results a sinus opening which occasionally discharges cheesy material, pus and blood The conversion of the dermoid to a sinus opening therefore results from subtotal surgical removal, or at times may take place spontaneously.

These midline dermoids of the neck may grossly resemble thyroglossal duct cysts. Thyroglossal duct cysts are remnants of the embryonic duct which connected the thyroid gland to the tongue The remnant of the lingual connection in adults is the foramen caecum in its posterior dorsal surface Thyroglossal duct cysts may appear as cystic masses on the posterior dorsal surface of the tongue.

Mucous Cysts. The so-called mucous retention cysts, which are situated on the inner aspect of the lower lip usually opposite the cuspid tooth, are very common (see Chapter 4).

Traumatic Epithelial Cysts. Cysts resulting from trauma are caused by (1) displacement of epithelial islands, (2) stimulation of epithelial growth or (3) production of alterations in the normal structure of cutaneous appendages such as the hair, sebaceous and sweat glands.

A traumatic cyst occurring under the free end of the fingernail may cause moderate tenderness and even erode the terminal phalanx by pressure. Ossification may occur within the cyst and necessitate removal

Sinuses and Fistulas. A sinus is an open channel, tract or tube, blind at one end and communicating at the other with a cutaneous or mucous surface A fistula [illegible], or between a cavity [illegible] granulation tissue or [illegible], tract is, for example,

[illegible] [illegible]illimeter-sized slitlike openings of congenital origin occur on the lower lip If bilateral, there is one opening on either side of the midline. The sinus tracts are generally 1 to 2 cm long and [illegible] blind pocket [illegible] to be

familial and are often accompanied by other deformities such as cleft palate and harelip.

The solitary midline sinus occurring on the upper lip just beneath the columella of the nose is the external manifestation of a deeper-lying dermoid cyst.

Epidermal Fistulas. In their simplest form epidermal fistulas are seen about the face, neck, buttocks and inner aspects of the thighs and less commonly about the breasts and axillae The process either originates in the double comedones of a severe acne vulgaris or follows a process similar to hidradenitis suppurativa.

Congenital auricular fistula, sinus preauricularis and fistula auris congenita occur as small papules situated at the anterior border of the ascending limb of the helix. From such sinus openings there may be an occasional offensive discharge. At other times with the closure of the orifice a retention cyst may develop in front of the ear. Finally secondary infection may convert the sinus tract or cyst into a walled abscess which opens either spontaneously or by incision In either event a solitary granulomatous lesion anterior to the ear ensues. As the result of repeated infections many fistulous tracts develop in an extensive area of skin This fistulous area may present a lesion which resembles lupus vulgaris or actinomycosis

There is a frequent association of preauricular sinus, a developmental defect, with other congenital malformations such as branchial fistulas of the neck, hypospadias and congenital absence of the tear duct

Sinus tracts of dental origin are common and are often associated with an alveolar abscess at the root of a tooth, less commonly with syphilis of the mandible and rarely with adamantinoma of the jaw They may open on the chin, the cheek, the floor of the nose, near the orbit and on the buccal or lingual aspects of the gums or at distant sites, as the neck

On the lateral aspects of the neck, sides of the face, and as high as the lower part of the eye may occur cysts which are remnants of an incomplete closure of an embryonic branchial cleft

Diagnosis of Cysts, Sinuses and Fistulas. Aside from the clinical findings, visualization of the tract and cysts by means of roentgenograms after the introduction of radiopaque solutions is a helpful measure In some cases much evidence as to the place of opening of a fistula may be obtained by the injection of a solution of methylene blue

Surgical treatment of some of these lesions may be difficult. A final diagnosis awaits histologic studies

INFECTIONS OF THE SKIN BY HIGHER ANIMAL PARASITES

Helminths. The term helminths is used to designate wormlike animals of three diverse phyla (1) Annelida (segmented worms), (2) Nemathelminthes (roundworms), and (3) Platyhelminthes (flatworms) In medical parasitology all parasitic worms are collectively referred to as helminths.

Annelida. The segmented worms are mostly free-living. The ectoparasitic *leeches* comprise the parasitic members of this phylum

The chief predators of man and animals are the terrestrial leeches that live in damp tropical forests, where they attach themselves to anyone within reach Various species have been described in southern Asia, the East Indies, Australia, Oceania and South America Aquatic species attack bathers, examples of these leeches are those that are encountered in the swimming holes along some southern streams and elsewhere in the United States

The bite, usually unnoticed, is detected by the presence of blood or the engorged leech The wound, though painless, bleeds readily because of the anticoagulative secretions of the leech and heals slowly. Heavy infestations of man and animals may result in serious exsanguination. A number of cases of infestation of

the upper part of the respiratory tract and of the digestive tract from drinking water have been reported Leeches in these locations after narcotization may be removed with foreceps Those attached to the exterior of the body may be removed after application of vinegar or strong salt solution to loosen their hold.

Creeping Eruption (*Hookworm Disease, Ancylostomiasis*). In man the skin lesions of creeping eruption are caused by penetrations of the larvae, commonly known as hookworms, of at least three species of nematode worms of the family Ancylostomatidae (superfamily Strongyloidea). *Ancylostoma duodenale, Necator americanus* and *Ancylostoma braziliense.*

The eruption develops after contact of the patient with moist sand and earth contaminated by the feces of infected dogs, cats or human beings At the point of invasion a reddish, itchy papule develops; and within two or three days narrow linear, slightly elevated, erythematous, serpiginous, intracutaneous tunnels are produced by the migration of the larvae, which move from a fraction of an inch to several inches each day. Vesicles form along their course, and the surface becomes dry and crusty. The itching is intense, and the resultant scratching may lead to secondary infection. The commonest site is on the hands or feet, but the eruption may occur on any part of the body It persists for several days or weeks.

Dracunculiasis. The Dracunculidae are long slender nematode worms, filarial parasites The definitive hosts, other than man, in North America are the fox, raccoon and mink The species parasitic in man is *Dracunculus medinensis* of the family Dracunculidae

When the infected cyclops is ingested in drinking water, the larvae penetrate the wall of the digestive tract and migrate to the loose connective tissues When the female worm reaches the surface of the body, it liberates a toxic substance into the subdermal tissues, producing a local inflammatory reaction in the form of a subacute sterile abscess with serous exudation and formation of blisters.

The early manifestations of urticaria, erythema, dyspnea, vomiting, diarrhea, pruritus and giddiness are caused by the absorption of allergenic substances from the worm If the worm is broken during extraction and the larvae escape into the subcutaneous tissues, a severe inflammatory reaction with fever ensues, and if secondary bacterial infection occurs, formation of abscess, sloughing of the tissues and even fatal septicemia may result.

The local cutaneous lesion appears at first as a reddish papule with a vesicular center and indurated margin The blister contains a clear, yellow fluid. The worm *lies in a subcutaneous tunnel with its anterior end beneath the blister.* Its course may be marked by induration and edema *Contamination of the ruptured blister* by pyogenic bacteria may produce abscesses, cellulitis, and ulcers. At times the worm may become calcified and remain for years as a hard, twisted cord beneath the skin

Diagnosis is made from the local lesion, worm and larvae Dead or calcified worms may be located by roentgenologic examination. Treatment involves the extirpation or destruction of the worm. The prognosis is usually good.

Cercarial Dermatitis. The cercariae, which are larvae of certain species of animal schistosomes or flukes (Platyhelminthes), produce in man a cercarial dermatitis.

The cercariae of 6 species of animal schistosomes have been associated with cercarial dermatitis: (1) *Cercaria elvae,* (2) *Cercaria stagnicolae,* (3) *Cercaria physellae,* (4) *Schistosoma deuthitti,* (5) *Trichobilharzia ocellata* and (6) *Schistosoma spindale* The first four are found in the United States of America.

In the United States *Cercaria elvae* and *Cercaria physellae,* found in swampy waters, produce *collectors' itch. Cercaria stagnicolae,* which frequents the shores of lakes, is more often the cause of *swimmers' itch.* Persons in contact with aquatic vegetation are most likely to be infected with *Cercaria elvae* and *Cercaria physellae.*

The affected beaches are usually near vegetation that furnishes a favorable habitat for snails The cercariae swarm in the shallow water or are swept toward the shore by wave action. They survive about 24 hours

Cercarial dermatitis has been recorded in England, France, Germany, Switzerland, the Federated Malay States, Canada and the United States of America. In North America endemic centers have been found in Saskatchewan and Manitoba, and in Wisconsin, Michigan, Minnesota and Iowa. Outbreaks have occurred in Illinois, North Dakota, Nebraska, Texas, Florida and Washington

The cercariae adhere with the ventral suckers and enter in about 5 minutes through the action of their anterior spines and lytic secretions Penetration of the skin occurs when the film of water evaporates The cercariae may remain alive in place for a day but the reaction persists around the burrows They may be destroyed in the epithelial layers of the skin and become walled off. During these actions there is inflammatory response with edema.

As the water evaporates, a prickling sensation is followed by the rapid development of urticarial wheals, which subside in about half an hour leaving a few minute macules After some hours severe itching, edema and the transformation of the macules into papules and occasional pustules occur, reaching maximal intensity in two or three days. The papular and sometimes hemorrhagic rash heals in a week or more, but may be complicated by scratching and secondary infection. Individuals vary in susceptibility

THE DERMATOSES

The term dermatosis is all-inclusive It simply means a skin disease. The term toxic dermatosis is all-inclusive too, for it refers to any skin disorder referable to a toxic agent. Still more tolerance is required in the use of these terms, for there are (1) the dermatoses due to a known or a proved group of toxic agents and (2) the dermatoses due to unknown toxic agents

The known agents which may produce dermatosis are: (1) bacteria, (2) some higher plant and animal parasites, (3) viruses, (4) chemical agents and (5) physical agents These agents have different methods of attack Some are able to attack directly while others attack indirectly The latter group make themselves manifest through sensitization, acting as allergens on an individual predestined by inheriting the weakness of being easily sensitized (see Chapter 18).

The various dermatoses are mentioned in their relation to a disease or in association with a toxic agent or agents in various parts of this text.

ENDOCRINE DISTURBANCES OF THE SKIN

Seborrhea. A definite etiology has not been established for seborrhea.

At puberty the adult distribution and type of hair develop and there is an increase, and perhaps a change, in the quality of the sebaceous secretion These changes are synchronous with puberty and are thus attributed to functioning of the glands of internal secretion It is in early adulthood that dandruff begins to be troublesome in some individuals

Seborrhea is often described as being of two types The dry type, or so-called *seborrhea sicca,* is commonly known as *dandruff*. The oily type is the so-called *seborrhea oleosa* It frequently is impossible to differentiate the two types. Seborrhea

with acne vulgaris The eruption appears as dull reddish erythematous patches, often with greasy scales, often well defined on the body, and it sometimes forms annular lesions over the sternum Itching may not be very annoying except just before retiring and during the night The patient may awake to find himself scratch-

ing the scalp. Occasionally the dermatitis extends down from the scalp or f hairline to the forehead. The patch may be well defined at its borders.

Acne Vulgaris. The disease is manifested as an inflammatory affectioı sebaceous glands. The characteristic lesions, the comedo, the papule, and the are distributed over the face, trunk and buttocks, where the sebaceous gla largest The lesions are painless unless severely infected. In boys the lesior often on the nose and chin synchronously with puberty, and in girls with tl of menstruation

The primary infection has been attributed to *Bacillus acnes* (*Coryneba acnes*) It is secondary invasion of the lesions by staphylococci that leads to ן tion. The altered sebaceous secretion in the comedones turns black on expc air. When a comedo is expressed, a small plug or wormlike mass of material or shoots from the follicle to be followed by thin pus Around the papule : pustule is well-marked hyperemia. Sometimes the pustules increase greatly and furuncles develop Chronicity results in deep scars which, on the face, : as disfiguring as those of severe smallpox. If occlusion of the follicular oן takes place, sebaceous cysts develop.

Acne is differentiated from the drug eruptions by the history Iodides, br and various estrogenic preparations or hormones taken internally, and tar, ן and chlorine, when applied externally, may produce lesions almost ident acne, although not always on the usual sites.

After the patient has reached the age of 30 years, acne vulgaris tends gradually and the scarring is less conspicuous by the time the age of 40 y reached

Rosacea. The occurrence of rosacea about the time of the menopause, the menopausal flushing of the face, is etiologically suggestive of an enc association

Rosacea differs from acne vulgaris in the absence of comedones, in distr and in age of incidence. Often rosacea begins in the late twenties, or the ons be delayed until the forties It commences as a chronic hyperemia of the face often terminates in a permanent dilatation of the capillaries. During the co this hyperemia papules, pustules and a patchy scaliness occur The distribu the disease is on the nose, cheeks, chin and forehead, especially between the

Rhinophyma is the advanced or the extreme stage of rosacea. Its worst festations are seen in alcoholics. Often the rosacea is accompanied by an er ment of the tip of the nose, which becomes irregularly bulbous, forming fleshy mass pitted with dilated follicles from which sebaceous material c expressed The organism *Demodex folliculorum* found in these dilated follicl no etiologic significance

Senile Dermatoses. As age advances, the skin loses its elasticity, becom wrinkled, lusterless, and seems too big. Warts that resemble flat warts, but u are larger and have a dark surface, often appear over the neck and the trunk growths do not become malignant

Senile keratoses, little, hard, persistent areas of scaliness on the face, nos hands, are evidence of the effects on the skin from years of exposure to sui wind The skin of those who have red hair is more susceptible and more ser to these influences than skin of other coloration The extreme of sensitivity is s in xeroderma pigmentosum, and similar conditions may be produced by roe rays or radium in a much shorter time. They are of the same nature, however all have a tendency to become malignant

Hypothyroidism. Deficiency in thyroid secretion leads to decrease in the s tions of the skin glands, and produces a dry skin with increase in the thickne the horny layer (xeroderma).

These skin changes are improved by thyroid therapy. Hypothyroidism ma

occasion be accompanied by an ichthyosis. The ichthyosis too is improved by thyroid therapy. However, a deficient thyroid plays no part in the etiology of ichthyosis.

Skin Diabetes. Urbach has defined skin diabetes as the syndrome of therapy-resistant, recurrent or chronic dermatosis, a high fasting skin sugar level together with a normal blood sugar curve, and pronounced improvement of the skin disease, as well as a drop in the high skin sugar level, on a low carbohydrate diet, sometimes combined with insulin.

In support of this view that there is a connection between the clinical syndrome and a disturbance in the carbohydrate metabolism, as in diabetes, are (1) the high fasting skin sugar levels, which attain and even exceed 80 mg per 100 gm.; (2) the pathologic and characteristically diabetic course of the skin sugar curve following oral sugar feeding; (3) the return to normal of the fasting skin sugar level, as well as of the skin sugar tolerance curve after a low carbohydrate diet, notably in combination with insulin.

On the basis of clinical experience, a diabetic diet should be tried in cases of therapy-resistant skin diseases such as furunculosis, eczema or pruritus, even when the blood sugar tolerance curve is normal

THE EFFECTS OF DISTURBANCES OF NERVE FUNCTION OR PSYCHIC CONTROL

Pruritus. Pruritus is an integral part of the symptom complex of a great many skin disorders The cause of the pruritus may be an obvious organic disease or it may be entirely of functional origin.

Pruritus Ani vel Vulvae. Pruritus ani and pruritus vulvae are, in the large majority of cases, purely of functional origin Rarely will diabetes or threadworms (*Enterobius vermicularis*) be found as causative factors Occasionally a local condition, such as a vaginal discharge, hemorrhoids, anal fissure, or an intertrigo, will be found

Neurodermatitis. A neurodermatitis occurs as a well-defined patch of thickened, lichenified skin, often scaly, and intensely itchy, which has been present for a very long time. These lesions occur where they are easily accessible to the patient, and therefore can be frequently rubbed, or where the clothing rubs Irritation leads to itch and scratching, which increases the itch, and results finally in the thickened crisscrossed patch

Senile Pruritus. This general itchiness of the dry skin of elderly people may be a most distressing condition and may gravely alter their physical and mental well-being

SKIN DISEASES OF UNKNOWN ORIGIN

Psoriasis. Psoriasis is a common, not serious, dermatosis of white peoples The lesions occur more frequently and more profusely on parts of the body that are covered with clothing than on parts that are bare They do not cause the patient discomfort

Men are more often affected by the disease than are women, and morbid heredity seems to be of etiologic importance Some families are more prone to the disease than are others Lesions of psoriasis may occur along the line of a cut or scratch, in a scar, or on areas such as the waist where clothing presses. Apparently [illegible]

for years to a patch on the elbow or knee, and then suddenly it appears on other parts of the body The disease may be active while the patient is well and disappear during an illness such as pneumonia, or during a pregnancy, only to return when the patient regains his normal state of health. In some instances an acute exacerba-

tion may be activated by a general nervous debility. Remissions occur, the patient remaining free from the disease for years.

Sunlight is beneficial to most of these patients. The lesions may largely heal after repeated judicious exposure to sunlight. The natural dislike for exposing the affected ugly skin to view, however, prevents many of the patients from obtaining an adequate amount of sunlight.

The lesion of psoriasis is a reddish, *slightly thickened area of skin, covered to* a considerable depth with a glistening silvery scale. This character of the scale may not be apparent at first sight, but it appears if the lesion is scratched. As the scratching is continued, the scale gradually comes away in masses or as a fine powder until its lowest layer is reached. This layer comes away in one piece as a soft scale and leaves a red shiny area dotted with tiny bleeding points. Removing the scale as described is truly the *scratch* test and is almost diagnostic in doubtful cases.

The size and shape of the lesions of psoriasis vary. Descriptive terms are used for the variations, among which are the following. If the lesions appear acutely as profuse eruptions of small, distinct and irregular patches, the condition is *psoriasis guttata*. The spots may enlarge into sizable patches, as in *psoriasis nummularis*. If the scales become heaped up, the disease is of the rupial form, *psoriasis rupioides*. In some cases the center of the lesion clears while the edge remains active and circinate or serpiginous, *psoriasis circinata* and *psoriasis gyrata*. The size of the patch is roughly indicative of its age, and in some long-standing cases the patches may cover large areas of the body and limbs. They may have a maplike appearance, *psoriasis geographica*. In all cases, however, the scratch test indicates the nature of the disease.

The lesions usually occur on the extensor surfaces, and almost always the elbows and knees and the scalp are affected sites. On the scalp the hair prevents the scales from being easily shed, so that the disease in this area is more easily discovered by palpation. Lesions elsewhere usually will make the diagnosis of scalp lesions clear; the resemblance of psoriasis to seborrhea is not great. Psoriasis may be found behind the ears and under the breasts.

The nails may be affected, giving rise to irregular thickening of one or more nails. There may be rows of punctate depressions in the nails. In cases of psoriatic arthritis the lesions of the nails are sometimes the only ones present.

In rare instances exposed parts may be affected, and lesions may appear on the face and hands. Psoriasis of the palms and soles may assume a pustular *form*.

In some instances psoriasis appears to be associated with rheumatoid arthritis. Both psoriasis and rheumatoid arthritis are common diseases and some of the apparent association may be due to chance.

In doubtful cases differential diagnosis is made more easily if the scratch test is used repeatedly. Syphilitic lesions give a feeling of greater thickening of the skin, are more reddish brown than psoriatic lesions, and show involvement of the face and the forehead. Circinate psoriasis simulates ringworm but the scales do not contain fungus. Seborrheic pityriasis of the scalp may offer difficulty, the localized, heaped-up patches of psoriasis, palpable to the touch, and the scratch test help to differentiate the two conditions. Psoriasis of the palms resembles a ringworm infection and so may psoriasis of the nails, so that examination of scrapings for fungus [illegible]. Psoriasis and lichen planus may resemble each other.

[illegible] a lifetime. An acute attack may

[illegible]

The laity does not know that the disease is noncontagious. The patients should be discouraged from use of public swimming facilities and from military service.

Lichen (Rubor) Planus. Lichen (rubor) planus is a rare chronic, benign disease occurring in middle aged individuals which may persist for the rest of their lives. It can and does appear *in an acute form with a generalized eruption* which is accompanied by itching. It may disappear spontaneously after weeks or months. Women are more frequently affected than men. The general health remai[illegible]

Itching is not often severe though it may become severe enough to interfere with sleep. Oral lesions may be painful enough to interfere with eating.

The lesion is a polygonal, flat-topped, shiny, crisscrossed papule which breaks the fine lines of the skin The papule varies in size, sometimes reaching a few millimeters in diameter, but agglomerations of papules may spread over a large area. The light lavender color is characteristic of the lesions and may be observed at the edges of chronic patches if the scales are wetted away. A feature of the disease is the occurrence of the lesions along the lines of the ribs or places of skin trauma, for instance, where a belt or a corset or other clothing rubs the skin.

The general appearance of the lesion varies considerably. The acute lesions consist almost entirely of papules. Variations in secondary characteristics have occasioned descriptions of the following forms of the disease.

The *bullous* variety is an acute form characterized by bullae interspersed with the papules. The *annular* variety is characterized by rings of papules caused by the regression of the central lesions and the appearance of fresh papules in the periphery. The *hypertrophic* or *warty* variety is the characteristic manifestation of chronic lichen planus. This form may resemble psoriasis if the characteristic papules and violaceous color at the edges are not evident The *atrophic* variety is rare The patches are ill developed and the macular lesions are purplish or white, frequently striated, and sometimes surrounded by erythema

The mucous membranes of the mouth or the vagina may be affected, giving rise to leukoplakia-like lesions, especially if the tongue is involved These lesions of mucous membrane often cause considerable discomfort.

The flexor aspects of the forearms and the fronts of the legs and around the knees and over the sacrum are favorite sites of eruption. However, the eruption may be widespread, especially in acute attacks.

The disease may run a short course of a few weeks or months, and the patient gets well It is the chronic form, with chronic warty patches giving rise to discomfort by their presence on the legs, in the mouth or vagina or on the glans penis, which most frequently is seen by the physician

The essential lesions of lichen planus and psoriasis are different and the distribution varies in the two diseases In lichen planus the papules are on the front of the forearms, and often there are patches in the mouth In psoriasis the knees, elbows and scalp are involved Chronic scaly patches below the knees are found in both diseases, and if no lesions are present elsewhere, the diagnosis depends on local characteristics. Psoriatic patches have little or no itch and have a shiny scaliness which gives a positive reaction to the scratch test (p. 512). Chronic patches of lichen planus are itchy, in some cases intensely so, *the scale is not easily* removed, and the violet color is characteristic

A patch of neurodermatitis may simulate chronic lichen planus. A neurodermite may be very itchy, purplish or brown, with adherent scale and cross-hatched with lines, but its distribution is somewhat different from that of lichen planus The neurodermite is usually where it can be reached easily The papules typical of lichen planus are not present in the lesions of neurodermatitis or elsewhere on the body, and the violaceous halo of the lichen planus patch is absent.

The lesions of mucous membrane must be distinguished from leukoplakia. The lesions of the mucous membrane, especially of the penis, or of the skin may resemble syphilis

Pityriasis Rosea. This disease resembles a dermatitis due to an infection It is most prevalent in young adults. The herald patch, which has been considered the primary lesion, can be identified in about 3 of 4 cases. It often occurs on the lower part of the abdomen or on the flanks. The herald patch *appears before* the rest of the eruption and may pass unnoticed since it is usually symptomless It is distinguished by its greater size.

The essential lesion, including the herald patch, is an oval, rose pink macule

which enlarges and sheds fine scales as the center clears, leaving scales at the periphery. The long axis of the patches on the body is generally parallel to the line of the ribs The lesions may vary in average size and a papular form may occur. Vesiculation is a rare occurrence.

The herald patch is followed in 2 or 3 days, sometimes longer, by the general eruption which often is confined to the trunk and the upper parts of the limbs General symptoms are seldom evident, though an initial low fever may be present Usually the eruption fades and in from 4 to 6 weeks from the onset has disappeared, although it may persist for months. The eruption is not itchy One attack is thought to confer immunity

The ringed scaly lesions may suggest ringworm, but fungus is not present Seborrheic pityriasis and syphilis do not offer much difficulty in differentiation.

Pityriasis Rubra Pilaris. This rare condition is characterized by the appearance of reddish papules corresponding to the hair follicles over the limbs and face and the middle phalanges of the fingers Elsewhere the eruption may closely resemble psoriasis From psoriasis it is differentiated by the scratch test

Exfoliative Dermatitis (Pityriasis). An exfoliative dermatitis is characterized by redness and profuse scaling of the skin. It may occur secondary to many skin conditions, such as psoriasis, pityriasis rubra pilaris, drug intolerances, and poisoning by heavy metals such as organic arsenical compounds In a great many instances it is a reaction to overtreatment of a skin disorder The patient often is obviously ill The disease runs a chronic course.

The exfoliation is first manifest on intertriginous surfaces as the axillae or groins, and spreads quickly, so that the entire integument may become involved The skin is thickened and red, and there is profuse desquamation of large lamellar scales The degree of severity of the eruption varies considerably The desquamation becomes less In severe instances the eruption lasts for months and, especially in the elderly, the disease frequently is fatal

Indeterminate Vesicular Lesions of the Hands. *Cheiropompholyx.* Cheiropompholyx appears as minute vesicles, often discrete, on the hands, along the sides of the fingers and in the palms of the hands, and on the soles of the feet. The vesicles come to the surface of the palms and fingers, burst and leave a raw weeping surface which heals slowly, and thus may be subjected to much irritation which impedes healing. The slow healing requires that the condition be distinguished from *ringworm infection A differentiation from an infective dermatitis* (infectious eczematoid dermatitis) cannot usually be made

NEW GROWTHS

Benign Growths. *Callosities.* Callosities are thickenings of epithelium due to friction, heat, pressure, irritation and perspiration They may occur on any part of the body which is subjected to the foregoing forces The hands are favorite sites, for instance, the "horny hand of toil," but the callosities occur on the knees of the devout, on the buttocks of the lazy, and on the feet of those who walk a great deal

Callus and Corns (*Clavus*) As a rule corns are the result of pressure and friction from ill-fitting shoes which crowd the toes together and force them into a hammer-toe position. Hammer toe itself may be free of corns. Faulty foot posture [illegible] of weight stresses on certain areas of the foot is another causative [illegible] the interphalangeal joints cause clavus

As the horny layers of the corn become thickened, the apex is forced deeper into the sensitive papillae of the corium, and discomfort and pain result. Objectively there is a circumscribed callus, which when trimmed away reveals a horny mass extending as a cone downward into the deeper areas.

Soft Corns. Soft corns occur on the lateral surfaces of and in the web between the fourth and fifth toes, and the bony prominence is nearly always on the base of the first phalanx of the fourth toe. They do not become hard and dry but are soft and elastic because of moisture and maceration; for this reason, they are called *soft corns*.

Verruca Plantaris. Plantar warts are infectious in origin; and once infection has occurred, they tend to spread to other parts of the foot. Plantar warts apparently seldom occur except at the site of a callus

Plantar warts are small circumscribed callus-like growths which form on the plantar surface of the foot and about the heel They are extraordinarily sensitive to pressure and thus may produce discomfort seemingly out of all proportion to their size. Plantar warts differ materially from callosities and corns. Shave off the top of the horny callous layer of a plantar wart, and a central core, composed of hypertrophied papillae, which is soft and vascular and has a marked tendency to bleed, will be found.

Fibromas. In the majority of cases fibromas arise from sebaceous glands The most marked type is seen in the molluscum fibrosum pendulosum or fibroma molluscum (Recklinghausen's disease), which, when extensive, may cover most of the trunk with large pendulous growths, sometimes cystic, at other times like emptied sacks, at others like small cystic swellings. These are often called neurofibromas, which they are not.

Osteomas. Osteomas of the skin are often secondary ossifications and often originate from injuries, inflammatory processes or tumors In rare instances osteomas of the skin occur as congenital abnormalities.

Keloid. Keloid is an overgrowth of scarred tissue. It may have resulted from (1) an intense inflammatory reaction or (2) innate susceptibility peculiar to certain skins It is more nearly related to the texture of the skin than to the color. Keloids are likely to follow burns These growths often occur in operative scars, even small scars, and tend to extend beyond the limits of the original scars In the beginning there may be pain and tenderness on pressure. In time, a year or two, a keloid tends to disappear.

Xanthelasma (*Xanthoma*) Xanthelasma is a form of xanthoma characterized by soft, light leather-colored or yellowish patches appearing especially on the eyelids near the inner canthi (see Diseases of Cellular Lipid Metabolism in Chapter 22). These yellow nodules in the skin have no relation to diabetes (xanthoma diabeticorum).

Keratosis Senilis. Over the face, neck, back and hands of aging patients appear flat, moderately adherent, slightly raised, yellowish-brown to dark-gray or almost black lesions When forcibly removed they show horny prolongations on their under surfaces Some families who have freckles are more prone to have these lesions than are others Keratosis senilis has little or no tendency to undergo malignant changes.

Malignant Growths. Epithelioma. Epitheliomas *of the skin comprise (1)* the basal cell type (rodent ulcer) and (2) the prickle cell type (squamous epithelioma).

lioma and nevocarcinoma)

RODENT ULCER The rodent ulcer, basal cell carcinoma, is the commonest malignant tumor of the skin These lesions, usually multiple, (1) arise at the junction of skin and mucous membrane, (2) originate as cystic growths, benign at first, and (3) arise in elderly persons, beginning as senile hyperkeratosis The sites of occurrence are usually near the eyelids, nose, and about the ears, but the tumors may occur on any part of the face or hands. Generally there is a history of a lesion which commenced as a small papule and enlarged slowly over a period of many years, growing much more rapidly after ulceration set in In cases of long-standing ulcerat-

ing lesions about the face, the superior maxilla and the nose may become deeply eroded. In these regions the ulceration may, if not checked, often penetrate into the nasopharynx or up into the eyeball, causing great destruction in these regions.

Although rodent ulcer may affect children, the growth usually commences when the patient is about 45 years of age or older. When fully developed, the lesion is a small ulcer with an irregular base and a rounded edge with white firm nodules occurring along the margins of the ulcer. Superficial lesions may partly heal and scar over. No discomfort is present until the deeper tissues are affected, when there are severe pains

In some instances this skin lesion will have the features suggestive of syphilis, lupus and squamous epithelioma The history of syphilis is shorter than that of rodent ulcer, and as the disease generally is tertiary when ulceration is present, a search of the skin is made for the presence of other scars and pigmentation Serologic tests of the blood and spinal fluid may be made as aids to diagnosis Lupus generally commences before puberty, and while there may be scarring, the clear reddish nodules are commonly evident and do not possess the typical rolled edge observable in rodent ulcer. Squamous epithelioma is much more rapid in its growth than rodent ulcer and may be accompanied by secondary enlargement of the adjacent lymph nodes, which are not affected in rodent ulcer.

SQUAMOUS EPITHELIOMA Epithelioma in the early stage often leads to difficulty in diagnosis. It differs from rodent ulcer in being more rapid in its spread, in showing no healed areas, and in producing, in time, secondary involvement of the lymph nodes

In early stages differentiation between benign and malignant lesions and in later stages distinction between basal and squamous cell carcinoma, as well as the identification of rare tumors, can be made by biopsy study Biopsy in suspected skin cancer is simple and virtually harmless (except in the cutaneous surface, in mucous membranes and in the eye)

The prognosis depends on the size of the lesion and the adequacy of the treatment Small localized lesions without invasion, 1 cm. or less in diameter, are cured in 9 out of each 10 cases When lesions are 1 to 2 5 cm. in diameter, without deep infiltration, less than one half of five-year arrests may be expected Lesions more than 2.5 cm in diameter, with evidence of invasion of muscle, bone or cartilage, or with involvement of regional lymph nodes, are rarely curable, but significant palliation can usually be obtained through the use of protracted roentgen therapy, by means of electrocoagulation or actual cautery, or by other appropriate palliative surgical procedures However, some five-year arrests can be expected

Malignant Melanomas (*Moles and Pigmented Nevi*). Malignant melanomas may develop from pigmented moles of the skin as the result of trauma naturally occurring as from clothing, shaving, or tight fitting shoes, and trauma from incomplete removal A melanoma may become actively malignant during pregnancy. However, generally a quiescent melanoma or mole simply becomes malignant suddenly and metastasizes to distant parts.

When malignant change takes place, the mole may increase in size, become raised from the skin surface and may become deeply pigmented. It becomes inflamed, shows a moist surface, and bleeding may occur Sometimes a black spot appears in the mole. Occasionally a number of pigmented nodules develop around it The lesion becomes ulcerated, and, as the disease progresses, the regional lymph nodes become involved In some instances multiple widespread malignant lesions seem to occur simultaneously.

In some instances lesions similar to melanoma may be present These lesions are almost without color. If color is present, it is a light brown These lesions occur as very small flat nodules or as bulky tumors These lesions are in sharp contrast to the intensely colored ones which are of an intense bluish black to black.

There are no reliable criteria for differentiating between benign and early malignant melanomas. In general, the harmless lesions are more likely to be light in color and soft; they may be papillomatous, and may be hairy. Alteration, darkening in color, increase in size, change in contour or texture, arouses the suspicion of malignant activity. The appearance of satellite melanotic tumors about the periphery of the original lesion is evidence that dissemination has already occurred

Biopsy of pigmented lesions is definitely contraindicated. These lesions should either be widely and deeply excised or left alone It is impracticable and inadvisable to attempt removal of all pigmented nevi from all normal individuals. In general, lesions subject to frequent trauma situated on the feet, genitalia or conjunctiva and in which there is objective evidence of growth, inflammation or itching should be excised Once a malignant melanoma has become disseminated, only palliative measures are available. Melanomas are generally but not always radioresistant

Sarcoma. Sarcoma involving the skin, but seldom arising from it, occasionally is seen in nodular form occurring on various parts of the body. These tumors are highly malignant, as evidenced by rapid formation, reddish color, and tendency to ulcerate easily These growths may be recognized early, but not soon enough, for the prognosis, irrespective of treatment, is bad.

Kaposi's sarcoma occurs as multiple hemorrhagic purpuric-appearing lesions generally affecting the lower extremities of persons between the ages of 40 years and 50 years The course is variable but is less hazardous than that of the single sarcoma

Kaposi's sarcoma has to be differentiated from purpura hemorrhagica by a study of the blood for those findings diagnostic of purpura (see the Purpuras in Chapter 12). The diagnosis is made by histologic study of biopsied material

SUBCUTANEOUS TISSUES

Diseases of the subcutaneous tissue are usually considered with those of the skin or of the more deeply situated structures, for, interposed as these tissues are between the skin and more deeply lying structures, they may be affected in disease of either

The Reticuloses. The term reticuloses designates those conditions of the skin which may affect the subcutaneous tissues through involvement of the reticulo-endothelial cells of the skin and the lymph nodes.

The reticuloses include the leukemias, the lymphoblastomas (Hodgkin's disease), mycosis fungoides and lipolemic reticulosis In the leukemias and the lymphoblastomas there occasionally are lesions of the skin, whereas in mycosis fungoides the skin manifestations are the characteristic feature of the disease.

In the reticuloses granulomatous lesions are relatively rare in the skin It appears that in the initial states the tissue reaction in the skin is more acute in type than that in the lymph nodes However, fibrosis and the development of Sternberg-Reed cells are seldom exhibited in the skin Lymph nodes, therefore, are far more promising leads toward histologic diagnosis than the skin. The eosinophilia in some cases may or may not be significant of an interrelationship with eosinophilic granuloma.

The cutaneous lesions, when present, in lymphatic leukemia and lymphadenoma consist of pruritus, urticaria, or a nodular, purple or reddish brown eruption A general exfoliative dermatitis may occur, especially in Hodgkin's disease. The diagnosis can be made only from histologic studies of sections of the affected skin.

Lipolemic Reticulosis. Lipolemic reticulosis may resemble Hodgkin's disease and other reticuloses The histologic changes in the lymph nodes are constant. There is disorganization of the normal structure of the nodes, though this is usually spotty In those areas the lymph sinuses are dilated, and often empty. There is proliferation of the reticular tissue, and many eosinophils and histiocytes are present Melanin is

present in large amounts, both free and in melanophores. Fat stains show considerable lipoid material

The usual clinical manifestation is a generalized lichenified or eczematous eruption of several years' duration, with darkening of the skin. In Negroes there may be depigmentation. Often there is loss of hair, especially of the scalp and axillae. Frequently there are changes in the nails, with thickening and discoloration and subungual thickening and hyperkeratosis.

Lipomas. Lipomas occur as lobulated or rounded masses in the subcutaneous tissue. They are soft and freely movable. When traction is made on the overlying skin, multiple small dimples form in it. Hard lipomas are designated fibrolipomas, whereas those having an increased vascularity may be called angiolipomas.

These tumors may occur anywhere in the body but are most commonly situated in the subcutaneous tissues over the back, shoulders, neck, thorax, abdomen and buttocks and legs. Other sites for lipomas are the mesentery, and serous tissues of the whole alimentary tract, kidneys, heart, uterus, meninges, respiratory passages and occasionally in the mouth and tongue

Lipomatosis. Multiple localized or unusual depositions of fat are classified as lipomatosis to distinguish them from the single localized fatty tumors and form of obesity. They cause little concern except from a cosmetic point of view or when they mechanically interfere with normal function because of being inopportunely situated so that function may be disturbed.

Heredity is an etiologic factor in the symptomatic progressive forms of lipomatosis. Lipomatosis of the pseudohypertrophic form of muscular dystrophy in which the adipose tissue invades between the muscle bundles causes some of the abnormal enlargement of the legs in these children. Lipodystrophia progressiva, a rare condition of girl children, is characterized by complete disappearance of subcutaneous fat above the hips and the development of psychoneurotic symptoms. In the nodular circumscribed lipomatosis the lesions are distributed as firm, discrete, freely movable subcutaneous tumors over the forearms, thighs and often the back. The diagnosis is usually obvious, but a biopsy study may be necessary for confirmation.

Adiposis Dolorosa (Dercum's Disease) Dercum's disease, or adiposis dolorosa, is a syndrome consisting of tender and painful fat nodules, often attaining large size, situated in the femoral and inguinal regions or in the cervical region. When the nodules are situated over smooth surfaces, the skin may become erythematous and stretched and tender. The patients are often partially disabled by weakness and apprehension

The disease is not an established entity in regard to etiology or pathology. It may last a long time, and during this time there is a gradual increase in deposits of fat and in the accompanying discomforts.

Fibromas. A fibroma is a circumscribed purposeless arrangement of fibrous cells. Fibromas are variable in size and consistency, some are soft and loose in texture, others are firm and hard to the palpating hand.

Fibromas may occur anywhere in the body. They arise in the skin, fascia and intermuscular tissues, about joints and in connection with nerves. They may be situated in the ovaries, breasts and uterus.

Fibromas of the skin are often multiple, hard and feel as though they were of subcutaneous origin. These tumors may hang as if on a stalk from the labia or anal margins (see Recklinghausen's Disease in Chapter 6).

Mycosis Fungoides. This is a rare condition, seen in persons more than 40 years of age. It is not a mycotic infection There is a scaly and extremely itchy eruption. The disease after months or years may form tumors which generally ulcerate and form a fungating mass. These scaly, itchy lesions and, finally, ulcerating masses, may affect the mucous membranes of the throat and intestines as well as all parts of the exterior surfaces The prognosis is grave.

DISEASES AND INJURIES OF THE BREASTS

Development. The earliest evidence of the development of the mammary gland is an epidermal ridge extending from the axillary region to the groin. Certain areas in this line thicken and form the mammary glands. This line is of interest chiefly because when accessory breasts form they are situated somewhere along its course.

When accessory mammary glands persist, most commonly it is the upper primary pair situated in the axillary region just over or beneath the edge of the lateral border of the pectoralis major muscle. These may share in the functional activity of the normally situated mammary glands. Accessory breasts may be observed first in the latter months of pregnancy when they prepare to lactate. In rare instances the accessory glands may become painful just prior to menstruation when the normally situated glands are free from pain.

The accessory mammary glands found in the axillary folds are of sufficiently frequent occurrence to make it necessary to remember them when considering the diseases of this region In instances in which there is a nipple associated with these accessory breasts, any disturbance here will be self-evident. In those instances in which there is no nipple, diagnostic difficulties may be encountered.

Normally developed mammary glands which will give milk may develop outside of the mammary line Such glands may occur on the thigh, buttocks or abdomen Accessory nipples (hyperthelia) without associated breast tissue may be found in the pectoral region and down the lateral aspects of the abdomen

Anomalies of Growth at Puberty. Frequently when the breasts are stimulated to growth at puberty, one responds at an earlier date than its mate and attains a considerable size while the other still retains the infantile state The importance of recognizing this condition lies wholly in the fact that the gland first to develop is normal and not malignant

Proof that the gland first developed is normal occurs when the previously undeveloped gland takes on growth and soon catches up with the other Why they may not simultaneously respond to the growth stimuli is not known

There is a sizable number of women who mature and bear children and who have well-developed nipples under which there is scarcely any breast tissue These women have a tendency toward an excessive amount of coarse hair on the face, around the nipples, in the pubic region and on the thighs. Their sexual desires are normal or excessive

Anomalies of Growth in the Mature Gland The mammary glands of different women vary greatly in size Why some mammary glands grow larger than others appears to be a matter of heredity Almost any size may be considered normal so long as the glands develop reasonably symmetrically Once their growth has ceased, as after the development of puberty, they may begin to grow again, a condition termed hyperplasia or *hypertrophy* Whether the enlargement is of fat or gland tissue is frequently difficult to determine In many of these cases the disturbances are esthetic only and depend on the viewpoint of the patient. The aging matron will tolerate with equanimity degrees of growth that would excite consternation in the maid In some cases the breasts become definite encumbrances. Instances have been reported in which the breasts reached the thighs. The development usually remains within the bounds of tolerance, particularly if the patient has attained advanced years Less commonly one breast only takes on excessive development. Such a breast is soft and compressible without any evidence of the presence of a tumor When the hyperplasia involves gland tissues, the breast may be not only larger but notably firmer

Often the overgrowth is due to an excessive development of fat In these fat breasts the glandular elements are sparse and will not perform their natural function if the individual undergoes the puerperium. In puerperium there is pain but no milk

Instead of producing disturbance at lactation periods, some overgrown breasts do so during the general disturbances of the menopause. Less commonly the fibrous tissue of an overgrown breast takes on elephantiasis-like development. In these cases the epithelial elements may also undergo hyperplasia and may give milk even in the virgin.

THE ADULT MAMMARY GLAND

The breasts gradually develop until they attain the form which they are destined to assume in adult life, varying much because of heredity. When they first reach their adult form, they are usually cone-shaped, carrying the nipples on their summits The breasts of some women maintain this form permanently, but usually when complete maturity is reached they become more or less pendent, varying much according to the nutritional state, the individual, familial and racial characteristics involved. The actual and relative size is subject to wide variations of no clinical significance.

When the adult breast is viewed in the sitting patient, it is in most instances somewhat pendent. At the apex the nipple protrudes, and about it is the areola, from which spreads in all directions the contour of the breast proper Thus the relations of the significant anatomic parts of the breast may be enumerated Each part now will be considered separately

The Nipple and Nipple Discharges. The external variations of the nipple are considerable The nipple may protrude but little, or may appear erectile even in repose. In the average instance it is a truncated cone, the surface of which is flattened, marked usually by pits or rugae or even a multitude of minute wartlike protuberances The nipple is capable of spontaneous elongation with puckering of the skin of the areola due to contraction of the circular nonstriated muscle fibers (erectile tissue) which surround the tubules The color of the nipple varies with the complexion of the individual In the blonde it is pale pink, and in the brunette dark pigmented. The color of the nipple and its environs usually become darker during the first pregnancy, a shade which in a measure is permanently retained

The appearance of the nipple depends somewhat on the position of the patient during the examination. A nipple that is normally protuberant in the recumbent position may seem to be retracted, particularly in pendent breasts, when the patient is sitting In some women nipples that appear retracted in the nonpregnant state may become normal in pregnancy In others they may remain retracted

The *nipple discharges colostrum* a short time before parturition (colostrum gravidarum). Regularly after parturition colostrum (colostrum puerperarum) can be expressed from the nipple. In some multiparous women colostrum can be expressed from the nipple between pregnancies. In all other instances discharges from the nipples are significant

Benign breast disease, which includes chronic cystic mastitis, fibroadenoma and papilloma, is the source of discharge from the breast in 3 of every 5 cases, whereas malignant breast disease, which includes Paget's disease, is the source of discharge in the fourth case No sign of a palpable breast tumor can be found in the fifth of either benign or malignant cases.

No one type of *nipple discharge* is specific for a particular type of breast lesion, and, conversely, cancer as well as benign breast disease can give rise to diverse types [illegible] of those who have [illegible] retion from the [illegible] tumors if they are not palpable.

Despite these facts, no one can afford to take the responsibility for pursuing the policy of watchful waiting without surgical exploration when a bloody discharge from the nipple is present

Scattered over the extent of the *areola* in a circular fashion are prominent elevations, due to the presence of the glandules resembling the racemose glands in structure In pregnancy they exude an oily liquid which should not be considered as a discharge from the nipple.

The Gland. The breasts present a variety of forms which vary with the position of the individual. A cone-shaped breast in the recumbent position is slightly pendent in the sitting posture. This form, being the average, is regarded as the normal after young girlhood has been passed.

The breast is composed of a series of from 16 to 20 primary ducts radiating from the nipple downward and outward. After forming the ampullae, the ducts then radiate toward the periphery of the breast The ampullae in turn end in lobulated cords varying much in size and complexity. Surrounding the lobules are connective tissue septa, which extend to the surface skin, forming all together a support for the gland lobules These are the ligaments of Cooper. They are important, for their contraction causes the dimpling of the skin in malignant disease and they determine the size and shape of superficial abscesses or the pointing of deep ones.

Most breasts are made up almost entirely of connective tissue with a sparse amount of fat. The termination about the border may be gradual, the fibrous tissue being interspersed with lobules of fat, but the borders may be uniform and terminate abruptly. Normal breasts may be so thick that when they are caught between the thumb and fingers they give the sensation of a heavy elastic pad Palpated with the flat hand, this gives the impression of a flat, soft tumorous mass suggesting a soft fibrosis. On the contrary, breasts may contain but little fibrous tissue, it being limited to little more than septa. Such breasts when palpated give the sensation of their main constituent, fat. The difference in palpatory findings in women of various ages is due to the changes in the character of the connective tissue rather than in its amount

The Lactating Gland. The changes in the breasts incident to pregnancy result from the increase in size due to the enormous development of the acini, the edema of the connective tissue and the increase in the circulation.

In some cases the new acini may develop beyond the fibrous regions similarly to the hyperplasia seen in the lower animals. This distribution of newly formed acini may be irregular, abundant in some areas, sparse in others. In others even in the late stages of pregnancy the acinar hyperplasia may be confined to the fibrous regions In the first months of pregnancy the breast shows congestion, and the superficial veins become dilated to such a degree that they form one of the early signs of pregnancy This is true at a time when there is little gross change in the gland itself

The Involutional Breast. The mammary gland undergoes recessive changes after the menopause If these changes are orderly, there is usually a general atrophy of the acinar and ductal epithelium and with this a lessening in amount and elasticity of the fibrous tissue In some breasts the atrophy of the acinar cells is preceded by a hyperplasia such as occurs in the mucosa of the uterus When this hyperplasia develops, it should no longer be classed as a normal involutional change. In most instances the hyperplasia subsides and the breasts then resume a normal recessive course. In a certain number of cases in which the hyperplasia persists beyond the menopause, the condition terminates in malignant disease

The topographic changes of the breast may be marked at or near the menopause because they respond to the physical change of the individual. Many women gain much in weight at this time and the breasts too gain fat However, as the emaciation of old age supervenes, the breasts share in the decline until only a flabby bag of skin and fat remains

Gynecomastia. The term gynecomastia refers to an enlargement of the mammary gland in the male When both breasts swell, there may be an endo-

crinologic cause such as neoplasm of the testicle or the administration of estrogenic hormone.

Gynecomastia was present in 5 soldiers in one group of approximately 20,000 troops (Sullivan and Munslow). In none of the 5 men was there an endocrine disease present, nor were there any associated endocrine disturbances, except that the condition had developed in 4 during adolescence.

More commonly the enlargement is due to inflammatory changes of a chronic type or to cystic disease somewhat similar microscopically to chronic cystic mastitis in the female. If only one breast is affected, a suspicion of neoplasm is aroused Symptoms may be absent or may consist of slight pain or discomfort. The unilateral tumors should be excised even if small, particularly because of the danger of cancer, which may occur in the male breast

Mastodynia. The term mastodynia connotes pain in the breast, which may be severe enough to be completely disabling This symptom is rarely due to an associated chronic cystic mastitis. Palpation of the breast reveals no abnormality This symptom has been designated as neuralgia of the breast and thought to be similar to the true neuralgias Treatment is unsatisfactory, mammectomy may not relieve the pain in the region of the breast.

INFECTIONS OF THE BREAST

Both acute and chronic inflammations of the breast occur.

Mastitis is classified as interstitial and parenchymatous Both types are usually preceded by cracking or fissure of the nipple or areola which admits microorganisms to the subcutaneous lymphatics Often the fissuring and invasion are the end of the process and if so, the mastitis is interstitial

Parenchymatous mastitis refers to those infections which are situated in the glandular and ductal portions of the breast The parenchymatous infections usually appear in the puerperium, from the fifth or sixth day onward. In marked contrast is the interstitial type which is common in the first days of the puerperium Either variety may end in suppuration with the formation of abscesses in various parts of the breast, necessitating drainage.

An occasional instance of mastitis is observed in the virginal or nonlactating breast during the course of some such disease as epidemic parotitis or after trauma

Acute Mastitis. *Formerly it was thought that Staphylococcus albus* was the cause of acute mastitis. More recently, however, it has been learned that *Staphylococcus aureus* is by far the commoner cause

Mastitis is always the result of infection. Either pathogenic bacteria from outside gain access to the breast through fissured nipples by way of the lymphatics, or some of the bacteria already present in the lactiferous ducts meet with *conditions* which enable them to invade the tissues

The symptoms of mastitis rarely appear before the end of the first week of the puerperium, and as a rule not until considerably later. Marked engorgement usually precedes the inflammation, the first symptoms of which are chilly sensations or an actual rigor, which is soon followed by a considerable rise in temperature and an increase in the rate of the pulse The breast becomes hard, its surface is reddened, [illegible] In many instances, by the end of 24 hours [illegible] without treatment; if the symptoms persist [illegible] to be expected

Abscess formation often causes pronounced constitutional symptoms with or without severe local symptoms In still another group of cases the process pursues a subacute or almost chronic course, the breast being somewhat harder than usual and more or less painful, but constitutional symptoms are either lacking or very slight Under such *circumstances the first indication of the true state of affairs is*

often afforded by the detection of fluctuation on examination of a caked breast (stagnation mastitis).

On examination the breast is swollen, tense, reddened, and tender when moved The pain and local tenderness indicate the situation of the acute process. When an abscess is present, the process may be *limited to a single quadrant. If the abscess is* not lanced, the breast is likely to become undermined in all directions, and, as a result, the destruction of tissue is extensive and numerous fistulous tracts form

The diagnosis of acute mastitis is obvious when there is a swollen, hot, reddened, tender and painful breast.

Chronic Mastitis. Chronic mastitis may originate in the breast during the puerperium and persist for a long time. The disease is often the sequela of abscess of the breast which has been poorly drained and in which fistulization is present.

Soon after the onset of puberty a diffuse enlargement of the breast occurs If the breasts be traumatized by handling or squeezing and stimulated by sexual excitement, a congestive condition may be initiated. This congestion may pass on to a true inflammation and suppuration

On examination the breast is somewhat enlarged and contains one or more irregular areas which are firm and tender. In the absence of a history of trauma in young women these areas should be biopsied for histologic study

Small localized alveolar abscesses occur in virgins. For a time there may be localized redness of the skin, milk, pain and soreness These abscesses usually resolve spontaneously

Tuberculosis. Tuberculosis of the breast may be the cause of persistent fistulas which have originated from what appeared to be an acute mastitis, abscess formation and surgical drainage. The first intimation that a tuberculous infection is present is often a failure to heal of the stab wound from the lancing of the abscess during lactation.

A certain number of instances of chronic mastitis, and particularly of chronic abscess formation, are of tuberculous origin. These instances, in which the onset is a slow enlargement in a quadrant of the breast, require separate consideration Tuberculosis of the breast occurs probably once for every hundred cases of carcinoma. Pregnancy and lactation are thought to be predisposing factors. It is usually unilateral and rarely exists in association with carcinoma

The disease begins as a painless irregular swelling in the breast. The skin becomes reddened There are no systemic reactions from the breast. Any systemic reactions are from a more profound tuberculous infection, for instance, in the lungs.

The breast is swollen and slightly tender, or there may be no tenderness and but little swelling. A lump or lumps are present. The nipple may be retracted. If abscesses have formed, the periphery of the tumor is hard, its center soft. The axillary lymph nodes may be enlarged on the side of the affected breast. Often nodes in both axillae are palpable.

The diagnosis is based on biopsy of the breast tissue. Without fistulization this form of tuberculosis of the breast is differentiated from carcinoma only by histologic study. Tuberculosis of the breast is usually primary, develops by direct invasion, and usually involves the regional lymph nodes The disease does not undergo regression, has no complications and is treated successfully by radical mastectomy. Drainage from a sinus tract should be submitted to microscopic and cultural studies for tubercle bacilli. Often there exists an underlying pulmonary tuberculosis

Syphilis. Gummas of the breast are rare. They appear as isolated tumors but are more frequently multiple and bilateral. Gummas may be subcutaneous but more commonly are intermammary. They can be diagnosed only by means of biopsy studies.

TRAUMATIC MASTITIS
(Fat Necrosis)

Injuries of the breast are commonly followed by necrosis of the fat in the injured region. This may continue as a solid reactive tumor terminating in resolution, or the center may break down, producing an aseptic abscess.

The trauma is usually an acute one, *for instance, the bite of a dog, a horse* or a sweetheart. Falls on the breast and injuries from being thrown against the steering wheel of an automobile are also common examples. Following the trauma there are soreness and tenderness. In other instances there is no history of trauma despite the finding of fat necrosis on histologic study

On section the center of the lesion is whitish, a color which contrasts with the yellow fat about When organization of the affected area is well in progress, the whitish hue may be obscured by the process of fibrosis The center may have undergone liquefaction, producing an irregular cavity of small dimensions compared with the bulk of the palpable tumor

The tumorous mass is continuous with its environment. It is hard The skin is not freely movable over it and may be reddened and edematous There is no dimpling of the skin, and the nipple is not retracted unless it was so before the disease began, nor is it fixed The tumor does not have the firmness of cancer

The diagnosis is usually obvious from the history and the examination but it is not certain until biopsy study is made.

PAGET'S DISEASE OF THE BREAST

Paget's disease is defined as a malignant papillary dermatitis affecting the areola and the nipple. Arising first as a superficial dermatitis, the chronicity, the feeling of thickening, and the unilateral character are the chief points worthy of note. The disease appears commonly after the menopause and may simulate an infective dermatitis. It is often exceedingly difficult to distinguish between the two conditions On the whole, the infective dermatitis is moister and not so circumscribed, but above all it yields readily to treatment. In Paget's disease the lesion is more definitely thickened and circumscribed and may show some retraction of the nipple. When allowed to continue, the condition spreads into the breast and subsequently to the lymph nodes of the axilla.

Biopsy is performed in all cases of suspected Paget's disease of the nipple which *does not clear up in a week or two after a program* of cleanliness and protection of the breast.

Paget's disease of the nipple is treated the same as any other carcinoma of the breast, by radical mastectomy Since many of these tumors are slow to metastasize, the prognosis is particularly good in patients without obvious metastasis

BOWEN'S DISEASE OF THE BREAST

Bowen's disease is characterized by the formation of a thick pinkish tubercle or papule covered by a thickened horned layer of skin In contrast to Paget's disease, Bowen's disease occurs on any part of the mammary skin and when malignancy *supervenes it is of the squamous epithelial type.*

BENIGN CYSTIC TUMORS OF THE BREAST
(Endocrine Disturbances)

Chronic Cystic Mastitis. This disease is called also Schimmelbusch's disease, chronic *interstitial* mastitis, chronic lobular mastitis, cobblestone breast, nodular breast, mastoplasia, mastopathia, cyclomastopathy and adenosis.

Chronic cystic mastitis, in spite of its designation, is probably not an inflammatory disease at all but is secondary to hyperplastic changes instigated by endocrine

activity The cause of these changes in the breast is now generally considered to be an abnormality in the cyclic activity of the female sex hormones. An essential feature of this disorder is the failure of normal involution, so that by repeated stimulation at each menstrual cycle, during pregnancy, and perhaps also by sexual excitement, the hyperplastic changes outstrip the hypoplastic or involutional process

The most important pathologic changes consist of a hyperplasia of the acinar and the ductal epithelium, particularly the latter, and a hypertrophy of the firm translucent hyaline tissue surrounding the ducts There may be varying degrees of round cell infiltration, which is the only histologic feature which points to inflammation. The hyperplasia in the ducts may produce obstruction or may be accompanied by excessive secretion, thus producing cysts. In some instances the hyperplastic ductal epithelium takes the form of papillary ingrowths into the lumen of the duct, intraductal papilloma, or into the lumen of a cyst, intracystic papilloma

Very few women who have chronic cystic mastitis ever consult a physician; if they do, they complain of a lump, or pain, or of discharge from the nipple.

The pain is usually slight and brings the patient to the physician only because it has aroused a fear that such a symptom may be a sign of cancer, even though no lump may have been felt. Actually, of course, pain is not a manifestation of cancer except in the terminal stages when ulceration and infection have occurred. Indeed, severe pain is generally indicative of the presence of other lesions, such as acute mastitis or abscess. The pain in chronic cystic mastitis is rarely constant, being worse at some period during the menstrual cycle, usually just before or during the flow. In a few patients, however, the pain may be severe enough to be disabling and demand relief; under such conditions it is called mastodynia (see p. 522).

Discharge from the nipple in chronic cystic mastitis is relatively uncommon, being encountered in less than 10 per cent of cases. In a study made by Hicken the discharge was bloody in about half the cases, and serous or greenish brown in the remainder. In ductal papillomas the incidence of discharge is much higher and the excretion is usually bloody; for example, Geschickter noted a bloody discharge in 47 per cent of 204 cases studied. When ductal papillomas are in or just beneath the nipple, they may be palpable, but when located in the depth of the breast, they are rarely palpable because of their small size A significantly large proportion of ductal papillomas undergo malignant change.

In a breast which is the site of chronic cystic mastitis a diffuse nodular or shotty sensation will be encountered on palpation of the parenchyma. This will be particularly apparent in thin pendulous breasts in which palpation is not impeded by a thick layer of subcutaneous fat. Often the lateral margin of the breast parenchyma will be felt as a sharp firm edge Both breasts are affected, and often equally so. When a single lump is felt, it is firmly attached to the rest of the breast parenchyma, and cannot be outlined as a separate tumor. In many patients, however, the differentiation between an actual tumor and a localized region of cystic mastitis may be made only after excision. On repeated examinations it will often be noted that the nodules vary in size and in the degree of tenderness at various periods during

... extends to the

pectoral muscle

The lump may be single, but if moderate in size it is usually due to a large cyst, more often the lump is rather small and in reality represents a portion of a diffusely nodular breast which for some reason becomes locally more prominent or nodular than the rest of the parenchyma. In many cases, however, the patient believes she feels a lump, but on examination only a diffuse nodular parenchyma is made out

[illegible] of one of the tumors

Single Cyst of the Breast. [illegible] cysts are encountered whi[illegible] no other symptoms However, in some instances serous or serosanguineous nipple discharges may be present On examination, although the contents of the cyst are serous, they are under so much pressure that they are as firm as a solid tumor, often imparting a hardness that arouses suspicion of carcinoma The walls of large cysts of this type present a bluish translucent appearance when exposed at operation; the term blue dome cyst has been given to such a lesion by Bloodgood. The diagnosis is made only by thoroughly examining numerous sections of the excised tissue.

A *galactocele* is a true retention cyst, due to obstruction of a duct, and contains retained milk. It is relatively rare and has little clinical significance because it usually empties spontaneously If it does not empty, the contents will become inspissated, removal may then be indicated.

BENIGN SOLID TUMORS OF THE BREAST

The breast may be the site of any of the tumors, such as adenoma, lipoma, fibroma and angioma, which are found in skin and subcutaneous tissue

Adenoma (Adenofibroma). Adenofibroma is a tumor of early adult life, often appearing in girls just after puberty and in young women. If the patient has known of the existence of the lump for a number of months or years, she may notice a definite, though slow, increase in size. Only rarely are the tumors multiple. Rapid growth may occur during lactation, owing to the same stimulus which affects the rest of the breast; many women, indeed, first notice the lump during such a period

It is thought that this tumor may have a similar origin to that of the adenomas of the thyroid If this should be true, adenomas of the breast may be classed not as neoplasms but as a result of endocrine stimulation

Adenomas contain more fibrous than epithelial elements. The adenomatous tissue may be so slight as to form single layers of epithelial cells surrounded by great masses of connective tissue, thus giving rise to the term intracanalicular fibroadenoma. Mucoid degeneration may occur, and then the tumor is designated adenomyxoma The microscopic structure sometimes bears a resemblance to that of chronic cystic mastitis

Until a lump is discovered, usually accidentally, symptoms are absent. Pain and nipple discharge are occasionally present In most instances the patient feels the mass while she is bathing, or notices it on examining her breast after some slight trauma This latter fact accounts for the frequent belief on the part of patients that the tumor followed an injury to the breast. Many women, however, now palpate their breasts regularly because of the lay propaganda conducted by the American Society for the Control of Cancer.

On examination a firm tumor, which is movable and distinct from the breast parenchyma, is palpated. The mass is usually larger and more definite than the lumps characteristic of chronic cystic mastitis.

A definite diagnosis cannot be made with certainty on palpation alone A decision, therefore, must be made in each case as to the indications for surgical intervention When a breast is removed from a young woman, she feels that a barrier has been placed between herself and a fundamental object in life. Realization and adjustment for her always involve the deepest forces of her personality. This is true not only of the young woman but even of those of advanced age, years after the breast has performed whatever function it may or may not have been intended to perform.

Operation is not indicated for a benign solid tumor of the breast if the tumor is not painful and is present in a young girl. In general, surgical excision is indicated in most women more than 25 years of age and in every woman more than 35 years

of age who has such a tumor. Excision and microscopic examination permit of a correct diagnosis.

Brodie's Disease of the Breast. The term Brodie's tumor should be reserved for large, excessively cellular and long-neglected fibroadenomas. The history of a pre-existing breast tumor of many years' duration which at first grows slowly or not at all and finally in recent months increases rapidly in size is the outstanding feature of Brodie's tumor The skin overlying the tumor is mobile, and the lymph nodes are not usually involved Enlargement may be so great that ulceration of the skin occurs from pressure necrosis, and the foul, fungating mass suggests a carcinoma. Sometimes the correct diagnosis of an innocent large tumor is impossible until the breast is removed and histologic studies are completed

Papillomas of the Duct. A serosanguineous discharge from the nipple often is characteristic of a papilloma in the lacteal ducts The bleeding from the nipple may be unaccompanied by any other symptoms for a period of several years. Bleeding may start from a slight trauma or spontaneously, and it may continue daily with the passage of a few drops or intermittently every 1 or 2 months. In some this symptom may become more persistent at the time of the menopause. Papillomas of the duct may occur in aging men.

On examination not more than one half of these patients will have a palpable tumor. On histologic study of the cyst it may be found to be either benign or malignant.

Lipoma. Lipomas of the breast are completely benign tumors. They cause trouble mainly from worry and anxiety of the patient because of their presence. However, no one can be sure that the tumor is a lipoma until biopsy studies are made.

Lipomas occur in the same age groups as carcinomas Gynecomastia excluded, lipomas are the commonest tumor of the male breast Lipomas do not originate in breast tissue. They begin in the subcutaneous tissue above the breast or in the submammary tissue along the lower border of the pectoral muscle and displace the breast forward

Lipomas may be soft, superficial, and apparently situated on top of the mammary tissue They may be lobulated on palpation and may cause dimpling of the skin When situated along the lower border of the pectoral muscle their identity is less easily recognized

MALIGNANT TUMORS OF THE BREAST

Carcinoma of the breast is predominantly a disease of women (100 : 1). It comprises more than 90 per cent of all malignant tumors of this gland; sarcoma comprises but 3 to 5 per cent

More than half the women who have carcinoma of the breast are more than 50 years of age Other than aging there is nothing known of the etiology Thus, the relation of chronic cystic mastitis to cancer is not known However, cancer develops in less than 1 per cent of the cases Experimental cancer has been produced by repeated injections of estrin, the significance of this fact is not known The relation between skin irritation in Paget's and Bowen's diseases and cancer is more definitely significant Trauma and previous lactation have no proved etiologic connection with the disease

Pathology Cancer of the breast arises from the ductal epithelium, or from acinous tissue. The various types of carcinoma of the breast are classified according to the relative proportion of fibrous and epithelial elements, the rapidity of growth, and particularly the microscopic arrangement of the cancer cells, for instance, their tendency to form definite glandlike structures Thus three main types are described. medullary carcinoma, scirrhous carcinoma and adenocarcinoma

Medullary carcinoma is a cellular and, in general, a rapidly growing tumor. It is soft, and it is more frequently found in young women than in those of more advanced age

Scirrhous carcinoma is composed largely of fibrous tissue. The large amount of fibrous tissue gives the tumor its characteristic stony-hard sensation on palpation It about equals medullary cancer in frequency of occurrence but its victims are women of more advanced age. It grows more slowly and tends to metastasize late

Adenocarcinoma derives its name from an arrangement of cells in the form of alveoli or acini. These tumors vary in their rate of growth. Some grow rapidly and metastasize widely Others are present for years before metastasis occurs. The tumor may invade the skin early and produce extensive ulceration. Colloid carcinoma is a relatively rare form of adenocarcinoma in which much colloid material is present.

The extension of cancer of the breast is by direct permeation into small lymphatic channels of the mammary lobules and into the subcutaneous tissue, fascia, muscle and skin. Once the tumor cells are in the lymphatic structures of the skin, the permeation is made evident by small nodules just beneath its surface. This condition is commonly a manifestation of local recurrence of a tumor after surgical removal has been attempted Tumors situated in the medial half of the breast involve the parasternal lymph nodes. Extension along fascial lymphatic channels which penetrate the pectoral and the upper end of the rectus muscles and the thoracic wall is common.

Metastasis through the larger lymph channels occurs to the regional axillary lymph nodes and occasionally to the supraclavicular nodes. In many, metastasis occurs by way of the blood stream to the liver, and to the spinal column and long bones. Metastasis to the liver may spread quickly and produce an abdominal carcinomatosis with all of its dire consequences. In some instances of cancer of the breast metastasis will appear in the ovaries (Kruckenberg tumor)

Classification of Cancer of the Breast. Surgeons have employed various criteria based on clinical or pathologic manifestations, singly or combined, in an effort to predict curability or incurability by surgical treatment. The classification arranged by Portman is adapted for use here. The indications for different therapeutic procedures for cancer of the breast and the general average of results as reported in the literature may be discussed on the basis of the classification and criteria of incurability presented.

In Portman's classification four stages of the disease are recognized and set forth as follows

First Stage. The earliest clinical sign of a cancer of the breast is a small, freely movable tumor without skin involvement, palpably enlarged lymph nodes or evidence of remote metastatic lesions. There are other tumors of the breast presenting the same clinical signs which are not cancers, therefore it often is impossible to make a differential diagnosis Microscopic examination is necessary

About 15 per cent of patients whose lesions have been considered to be of stage 1 after operation and microscopic examination die within 5 years The reasons probably are: (1) Neoplastic cells may not have been arrested in axillary nodes but may have passed through them and metastasized elsewhere, presenting no clinical or pathologic evidence prior to operation (2) The cancer may have metastasized not to the axilla but to the internal mammary or mediastinal groups of nodes, as happens especially in the case of inner quadrant tumors. (3) Metastatic lesions may not have been detected by microscopic examination

Second Stage The second stage in the progress of cancers of the breast usually embodies a movable tumor without skin involvement but with metastatic extension in a few axillary nodes, none being demonstrable elsewhere The prognosis after operation is almost in direct ratio to the relative number of nodes involved About 25 per cent of patients who undergo operation will have only a few nodes involved (stage 2), and the general average of five-year survivals has not been more than 50 per cent by operation alone

within 5 years, it must be because extension had taken place beyond the anatomic limits of surgical removal Although recurrences seldom take place locally in the chest wall or in the axilla of those who have undergone radical mastectomy, the disease probably has extended to the infraclavicular or supraclavicular and parasternal nodes and eventually will spread to vital organs It would seem logical to give postoperative roentgen therapy in such cases in order to delay the progress of the residual cancer. This will be accomplished in about 15 per cent of cases.

Third Stage. The third stage of cancer of the breast includes cases with metastatic lesions in many axillary nodes, skin involvement (dimpling) and with or without other criteria of incurability. In some cases in the latter classification the presence of metastatic *involvement in many axillary nodes can be determined only after operation.* The prognosis is little if any better in such cases than in those with criteria of incurability. However, most cases in stage 3 will be classified as having these criteria

The general average of five-year survivals by operation alone for stage 3 cases has been about 5 per cent. It has been found that the average natural life expectancy of women with cancer of the breast who have received no treatment is almost 3 years, and 5 per cent live 5 years Therefore, it may be concluded that radical operations for stage 3 cases do not increase survival rates

Fourth Stage A fourth class of cases of cancer of the breast must be made to *include those with remote metastatic lesions on initial examination, regardless of the* presence or absence of criteria of incurability A complete physical examination and a roentgenographic survey of the lungs, skull, vertebrae and pelvis should be made of all patients with tumors of the breast to exclude the possibility of metastatic lesions before therapeutic procedures are instituted, especially when there is a suspicion of cancer. Metastasis to these regions or other viscera may develop from cancers which appear to be clinically in early stages Patients with remote metastatic lesions are not wittingly submitted to operation, and the majority are treated for palliation by irradiation or other measures such as endocrine therapy or by both In one series 20 per cent of patients *were found on initial examination to have remote metastatic lesions*

It should be noted that about 45 per cent of all patients observed by Portman were classed in stages 3 and 4 combined, when first examined Such cases are incurable, and the average of five-year survivals after operations alone is no greater than if no operation were performed—perhaps less

Examination A carcinoma of the breast is a firm, often hard, tumor that cannot be separated from the surrounding breast tissue or moved within this tissue. The contour, the size, the shape and the nipples of the breasts are compared. An indentation or a bulge in the contour may reveal the site of a lesion The contour of a breast may be altered by the height of the two breasts on the chest wall and their relative size

Very commonly one breast is the larger of the two If the general contours of the two are the same, the difference in size usually is normal, being a developmental difference

The shape of the nipples and the axes in which they point are compared The surface of the nipples is inspected for evidence of crusting or erosion.

The enlarging carcinoma fixes the fascial septa of the breast, exerts an abnormal traction on them, sometimes pulls the skin inward to produce dimpling, and deviates the axis in which the nipple points, or flattens and retracts the nipple If the carcinoma has extended sufficiently to be attached to the pectoral fascia, the pectoral muscle may be contracted, the sector of the breast in which the carcinoma lies is pulled upward abnormally, and its contour is distorted The horizontal levels of the areola and nipple are often elevated by a carcinoma in the upper half of the breast

Deviation of the axis in which the nipple points is a subtle sign of retraction The fibrosis in and about the carcinoma pulls on the ductal system and tilts the nipple so that it points toward the carcinoma.

When the carcinoma involves the area beneath the nipple, the fibrosis shortens

the whole ductal system and pulls the nipple inward. This process may reveal itself as flattening and broadening of the nipple on the side of the carcinoma As the fibrosis progresses, the nipple becomes flatter and broader until, in some instances, it is finally retracted beneath the surface of the surrounding areola.

Dimpling of the skin over a carcinoma of the breast may be demonstrated in some cases by the patient's raising her arms high above her head. However, dimpling is most easily and uniformly demonstrated by gentle compression of the breast between the hands

The relative degree of fixation of the carcinomatous region in the breast to the pectoral fascia is best demonstrated by determining the amount of lateral excursion of the tumor, while the patient lies supine, by gently moving the tumorous portion transversely across the chest wall between the fingers of the examiner's two hands, first with the patient's arm relaxed and then with her hand pressed against the hip to contract her pectoral muscles

Supraclavicular and Axillary Regions. During the examination of the supraclavicular regions the patient sits facing the examiner. The supraclavicular space is palpated with the ends of the fingers. Nodes in this region are often softer than those in the axilla.

In the examination of the axilla, ask the patient to place her hands on top of her head while the lower limits of the axilla are examined Then have her lower her arms to her sides while the upper limits of the axilla are examined with the tips of the fingers The right axilla of the patient is examined with the left hand The left axilla is examined with the right hand Lymph nodes high up in the axilla are difficult or impossible to feel Nodes lying close behind the thick body of the pectoralis major muscle as it forms the ventral wall of the axillary space are also difficult to palpate In obese patients palpation of the axilla is particularly unreliable

The number, consistency and movability of the axillary lymph nodes are observed The nodes may be fixed to the underlying axillary structures or to the overlying skin. The transverse diameter of the largest axillary node is estimated in centimeters

Palpation is inaccurate in determining whether or not axillary lymph nodes contain metastatic lesions These nodes may enlarge from causes other than malignant disease

Diagnosis The diagnosis of cancer of the breast is often obvious from the presence of one or more of the foregoing findings If these findings are definite, the carcinoma has reached an advanced stage It is desirable to find a tumor in the breast so small that biopsy is indicated for making a positive diagnosis. Histologic study is the certain way of making a correct diagnosis

Early in the course of cancer of the breast metastasis tends to take place to the cervical and axillary lymph nodes, ribs and spinal column, liver, pelvis and abdominal viscera; and the skin

Bilateral Cancer of the Breasts. Bilateral cancer of the breasts occurs frequently enough so that the presence of a known cancer of one breast requires study of the other breast, particularly if there is a lump in the second breast Bilateral carcinoma occurring simultaneously is rarely found, but it does happen The carcinoma of the remaining or second breast may occur years after the first one has been removed Often it is difficult for the pathologist to be positive whether the malignant lesion in the second breast is primary there or secondary or metastatic from the first breast involved

Inflammatory Carcinoma of the Breast. Inflammatory carcinoma of the breast implies the coexistence of carcinoma and inflammation. The fact is, however, that these breasts usually do not contain evidence of inflammation on histologic study. The condition often occurs in lactating breasts, but this incidence is by no means constant.

Pain is a commoner first symptom in the so-called inflammatory carcinoma of the breast than in the usual instance of carcinoma

Physical examination reveals diffuse induration extending through much or all of the breast. So dense is the inflammation that often a definite tumor cannot be palpated.

Inflammatory carcinoma frequently enlarges the breast Enlargement of one breast may be the first intimation of trouble. The skin of the breasts is red and often edematous Axillary lymph nodes are always palpable. Despite extensive involvement of the breasts, ulceration of the skin is rare. When present, it occurs very late in the course of the disease. All studies on inflammatory carcinoma of the breast indicate a poor prognosis.

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Part Two

The Systemic Diseases

In medicine, the term system has one of three meanings (1) a set or series of parts or organs which unite in a common function; (2) a whole bodily organism which unites in a common function and (3) a school or method of practice.

In this part of this book the first meaning is applied. Hence, the term systemic disease refers to disease affecting one or all parts which are related to perform a certain function; for instance, disease of the lungs, trachea, bronchi, and pleura, one or all of them, is disease of the respiratory system

9

DISEASES OF THE THORACIC WALL, PLEURAE, MEDIASTINUM, BRONCHI AND LUNGS

THE THORACIC WALL

The lungs and heart may be hampered in the performance of their functions by diseases of their own as well as by being influenced by diseases of the body as a whole. Hence the condition of these organs often serves as a guide to the general bodily functioning, and therefore the state of the respiration and circulation is continually being examined for purposes of diagnosis, prognosis and treatment It is for these reasons that the physical examination of the thoracic organs occupies a prominent place in diagnosis by physical means. Once a physician has gained even moderate skill in examination of the thorax he has gone a long way on the road of rendering good service to patients These statements do not imply that an examination by physical means is all that is necessary in diagnosing diseases of the thorax They simply mean that examination of the thorax by physical means is always necessary. At times the circumstances may be such that examinations by any other means are not feasible and then examinations by physical means may have to suffice for the basis of treatment.

Shape of the Thorax. The bony chest is subject to defects in development as well as to disease and injury and to deformities due to these causes.

The thorax is conical in shape, being small above and large below. In infancy the anteroposterior and the transverse diameters are nearly equal. At the age of 2 years the chest has become oval, and in adults the transverse diameter is one fourth greater than the anteroposterior

Variations in the shape of the thorax are mainly the result of disease. In childhood, rachitic disease (rickets) produces a lateral flattening and a projection of the sternum If the sternum projects markedly, it constitutes what is known as pigeon breast, the thorax in such a condition being longer from front to back than from side to side In this disease also there may be a depression on each side of the sternum, the back is rounded

ints of junction of the ribs and

what is known as beading of

from the level of the ensiform

cartilage a groove passes out toward the sides, this is known as *Harrison's groove* Sometimes the lower end of the sternum is pressed inward, forming a deep funnel-shaped depression constituting the deformity known as *funnel chest.* This shape of the chest may be produced in children by obstruction to the breathing from enlargement of the tonsils, from the presence of adenoid growth in the pharynx, and from hypertrophy of the

turbinate bones, all of which obstructions interfere particularly with nasal resp

Diseases of the lungs and pleurae ... of the thorax. These common tions ... the lungs and pleurae.

T ... *horax.* On inspection of the chest appea... rounded or flat. One side may be larger than the other, a intercostal spaces may be obliterated or retracted. The ... observed and recorded.

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the s ... pieces of the stern oppo ... *cartilage. It forms a distinct prominence, the a sterni* or angle of Louis.

The tip of the xiphoid or ensiform cartilage can be felt even in the obese p The top of the sternum is opposite the lower edge of the second thoracic ve The angulus sterni is opposite the fifth thoracic vertebra. The tip of the en cartilage is opposite the eleventh thoracic vertebra. Above the upper end sternum is the suprasternal notch or depression; below its lower end is the *sternal depression or epigastric fossa.*

The sternoclavicular joint possesses an interarticular cartilage betwee clavicle and the sternum which separates them sufficiently to allow the for of a distinct depression, which can be felt Below the inner end of the clavic first rib can often be seen and felt

The cartilage of the seventh rib is the last to articulate with the sternum tenth rib is the lowest which is attached anteriorly, the eleventh and twelfth shorter and floating ribs. The intercostal spaces are wider anteriorly than poste and the third is the widest

In men the nipple is usually in the fourth interspace or on the lower bor the fourth rib and on a line a little to the outer side of the middle of the cl In women the mammary gland reaches from the third to the ...

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Chapter 6

Directional Terms and Topography of the Thorax and the Respir Organs. For the sake of convenience in description and record, the t arbitrarily is divided into various regions and marked by longitudinal lines.

The Longitudinal Lines. Seven longitudinal lines are used. They run paralle the long axis of the body Three are situated anteriorly (Fig. 9-1) and two poster

1. The *median line* is the midline of the body. This runs down the middle sternum anteriorly and the middle of the back posteriorly
2. The *parasternal line* runs parallel to the edge of the sternum and midwa tween it and the midclavicular line
3. The *midclavicular line,* also called the *mammary line,* is a longitudinal line ing through the middle of the clavicle This usually passes ⅗ to ⅘ inch (about 2 cm.) medial to the nipple.
4. The *anterior axillary line* passes through the anterior fold of the axilla
5. The *midaxillary line* passes through the middle of the axilla
6. The *posterior axillary line* passes through the posterior fold of the axilla
7. The *scapular line* passes longitudinally through the lower angle of the sca

The Regions of the Thorax. In the middle of the surface of the thorax ante there are three regions.

1. The *suprasternal region* is the part above the sternum between the sternocl mastoid muscles. It is the suprasternal notch.
2. The *upper sternal region* extends from the suprasternal notch to a line d opposite the third costal cartilages.
3. The *lower sternal region* is behind the second piece of the sternum from third costal cartilages down

Anteriorly but *laterally* to the middle regions of the thorax there are four regions:

1. The *supraclavicular region*, above the clavicle. This includes the supraclavicular fossa.

2. The *infraclavicular region*, below the clavicle down to the upper edge of the third rib.

3. The *mammary region*, from the upper edge of the third to the upper margin of the sixth rib. This extends laterally from the edge of the sternum to the anterior axillary fold and has the nipple nearly in its center.

4. The *inframammary region* extends from the upper margin of the sixth rib to the lower margin of the thorax.

Laterally on the thorax between the folds of the axilla there are two regions:

1. The *upper axillary region* extends down to the upper border of the sixth rib

2 The *lower axillary region* extends from the upper border of the sixth rib to the lower edge of the thorax

Posteriorly there are four scapular regions.

1. The *suprascapular region* is above the spine of the scapula

2. The *scapular region* is the part covered by the body of the scapula below its spine.

3 The *infrascapular region* is the part of the thorax below the scapula between its angle and the lower edge of the chest.

4. The *interscapular region* is the part between the posterior edge of the scapula and the median line.

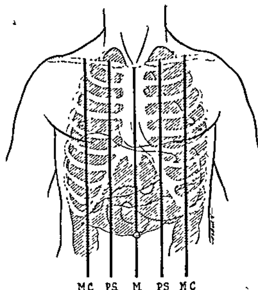


Fig 9-1 Topographic areas of the anterior thorax M C, midclavicular, P S, parasternal, M, median or midsternal When used, designate right or left side of patient

The Pleurae. These form closed spaces which line the thorax (parietal pleura) and cover the surface of the lungs (visceral pleura) The pleurae are completely in contact with the lungs only when the lungs are fully expanded In ordinary breathing the lungs are not completely expanded, hence the edges of the pleurae fall together and so prevent the formation of a cavity This collapsing of the pleurae takes place mainly along the anterior and lower borders of the lungs

The apex of each pleura is attached to the tip of the cervical fascia There is an attachment to the first rib and to the scalenus anticus muscle which prevents collapse (Fig 9-2)

The upward extension of the pleura is about on a plane with the superior surface of the first rib The posterior portion of the pleura is higher than its anterior portion at the anterior end of the first rib The pleura extends 1 inch (about 2 5 cm) above the level of the superior surface of the clavicle.

The top surface of the pleura is stretched in the form of a plane which is almost on a level with the superior surface of the first rib From the top the pleura slopes forward behind the sternoclavicular joint to meet the pleura of the opposite side at the level of the second costal cartilage The pleura covering each lung then descends to opposite or a little below the fourth costal cartilage, where it diverges toward the side, thence to the upper border of the seventh costal cartilage near its sternal junction, thence downward and outward to the lower border of the seventh rib in the mammary line, the ninth rib in the axillary line, and the twelfth rib posteriorly. The scapular line intersects the lower edge of the pleura at the eleventh rib.

The Lungs. When the lungs distend, they expand mostly downward but also, to a lesser extent, laterally and anteroposteriorly, owing to the elevation of the ribs which is due to the traction of the muscles upon them Breathing is performed mainly by the intercostal muscles and diaphragm As the diaphragm descends, the air is drawn into the

turbinate bones, all of which obstructions interfere particularly with nasal respiration

Diseases of the lungs and pleurae alter the shape of the thorax. These common alterations are considered in the section on examination of the lungs and pleurae.

Topographic Examination of the Thorax. On inspection of the chest it may appear normal, rounded or flat. One side may be larger than the other, and the intercostal spaces may be obliterated or retracted. The gross abnormalities are observed and recorded.

The clavicles and the sternum are subcutaneous and can readily be felt beneath the skin. The point of junction of the first and second pieces of the sternum is opposite the second costal cartilage. It forms a distinct prominence, the angulus sterni or angle of Louis

The tip of the xiphoid or ensiform cartilage can be felt even in the obese patient The top of the sternum is opposite the lower edge of the second thoracic vertebra. The angulus sterni is opposite the fifth thoracic vertebra The tip of the ensiform cartilage is opposite the eleventh thoracic vertebra. Above the upper end of the sternum is the suprasternal notch or depression, below its lower end is the infrasternal depression or epigastric fossa.

The sternoclavicular joint possesses an interarticular cartilage between the clavicle and the sternum which separates them sufficiently to allow the formation of a distinct depression, which can be felt. Below the inner end of the clavicle the first rib can often be seen and felt.

The cartilage of the seventh rib is the last to articulate with the sternum The tenth rib is the lowest which is attached anteriorly, the eleventh and twelfth being shorter and floating ribs. The intercostal spaces are wider anteriorly than posteriorly and the third is the widest

In men the nipple is usually in the fourth interspace or on the lower border of the fourth rib and on a line a little to the outer side of the middle of the clavicle. In women the mammary gland reaches from the third to the seventh rib

The operation of paracentesis, or tapping for pleural effusion, is often done in the sixth interspace in the midaxillary line or posteriorly (see Back in Locomotion, Chapter 6)

Directional Terms and Topography of the Thorax and the Respiratory Organs. For the sake of convenience in description and record, the thorax arbitrarily is divided into various regions and marked by longitudinal lines.

The Longitudinal Lines. *Seven longitudinal lines are used. They run* parallel with the long axis of the body. Three are situated anteriorly (Fig. 9-1) and two posteriorly:

1. The *median line* is the midline of the body This runs down the middle of the sternum anteriorly and the middle of the back posteriorly.
2. The *parasternal line* runs parallel to the edge of the sternum and midway between it and the midclavicular line.
3. The *midclavicular line,* also called the *mammary line,* is a longitudinal line passing through the middle of the clavicle This usually passes ⅗ to ⅘ inch (about 1 to 2 cm) medial to the nipple.
4. The *anterior axillary line* passes through the anterior fold of the axilla
5. The *midaxillary line* passes through the middle of the axilla.
6. The *posterior axillary line* passes through the posterior fold of the axilla.
7. The *scapular line* passes longitudinally through the lower angle of the scapula

The Regions of the Thorax. In the middle of the surface of the thorax anteriorly there are three regions:

1. The *suprasternal region* is the part above the sternum between the sternocleidomastoid muscles. It is the suprasternal notch.
2. The *upper sternal region* extends from the suprasternal notch to a line drawn opposite the third costal cartilages.
3. The *lower sternal region* is behind the second piece of the sternum from the third costal cartilages down

are not due so much to a bulging or to a retraction of the lungs as to the atrophy of the fatty and muscular tissue in tuberculosis and to the muscular tension in emphysema.

In coughing, the apex of the lung does not bulge into the neck above the clavicle, as it appears to do, but remains below the plane of the top of the first rib. The appearance of bulging is caused by the movements of the trachea in the median line and of the muscles laterally This is noticeable particularly in the platysma and omohyoid muscles In quiet breathing the posterior belly of the omohyoid lies about level with the clavicle, but in coughing it rises 1 or 2 cm. above it The intercostal membranes and muscles are kept tense by the constant elevation of the ribs due to the muscular tension.

OUTLINE OF THE LUNGS. *Apex.* The apex of each lung has its highest point opposite the posterior extremity of the first rib (Fig 9-2). It then follows the plane of the top of the first rib down to the sternoclavicular joint immediately above the junction of the cartilage of the first rib with the sternum The anterior end of the first rib is about 2 inches (5 cm.) lower than the posterior The upper edge of the clavicle is 1 inch (about 2.5 cm) above the anterior end of the first rib and 2 5 cm below the head of the first rib, hence the apex of the lung rises 1 inch (about 2 5 cm.) above the clavicle, and it lies behind its inner fourth This distance will vary in different individuals with the obliquity of the ribs The more oblique the ribs, the greater will be the distance between the level of the top of the clavicle and that of the neck of the first rib The top of the lung, however, never is above the level of the neck of the first rib There is no appreciable difference in the height of the right lung and the left lung (Fig. 9-3).

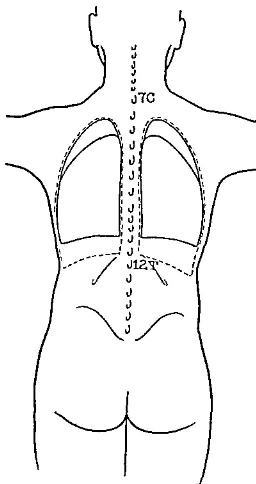


Fig 9-3 Outlines of the lungs—posterior view

Anterior Border. From the sternoclavicular joint the borders of the lungs pass downward and inward until they touch or almost touch in the median line at the angle of Ludwig opposite the second costal cartilage Below this the right lung extends a little across the median line and the left recedes slightly away from it. The right lung leaves the sternum opposite the sixth costal cartilage to which it has gradually descended

The left lung on reaching the level of the fourth costal cartilage curves outward and downward across the fourth interspace to a point about 1 inch (2.5 cm.) to the inner side of the nipple in the fourth interspace. From this point it goes downward and inward across the fifth rib and interspace to the top of the sixth rib about 1⅕ inches (3 cm) to the inner side of the nipple line This isolated tip of lung just above the sixth rib over the apex beat of the heart is called the lingula

Lower Border. The lower edge of the lung varies in different individuals, and in the same individual according to the amount of inflation In quiet respiration it

trachea and lungs, and the pressure within the thorax is lowered to zero or to a m[illegible] quantity, so that if it were not for its bony framework the chest would collapse. [illegible] framework is sufficiently strong to retain its shape despite this pressure if the breathin[illegible] normal and the thoracic walls are healthy. When, however, obstruction of the air passa[illegible] is present in young patients, the deformities funnel breast, pigeon breast or variations

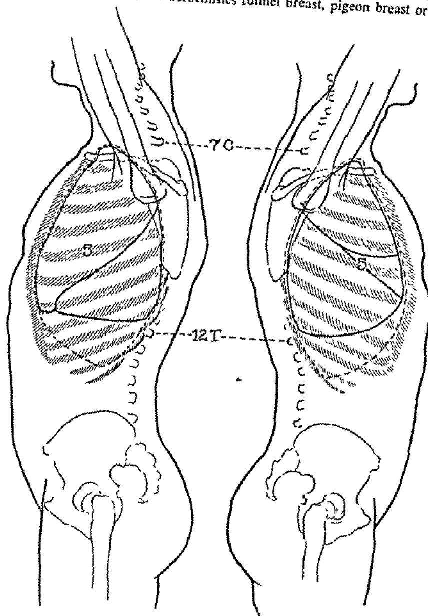


Fig 9-2. Lateral views of the extent of the pleura and outline of the lobes of the lungs

these are produced. These deformities are also produced by weaknesses in the bony thorax, such as occur in rickets

Enlargement of the chest posteriorly is impossible because of the support of the ribs, vertebrae, and strong back muscles. Enlargement downward is allowed by a descent of the diaphragm, hence the fullness of the abdomen in those affected with emphysema and, conversely, the flatness of the abdomen in those whose lungs are contracted In the region of the apices the thorax is closed by the deep fascia, which spreads from the trachea, esophagus, muscles and great vessels and blends with the pleura to be attached to the first rib. In disease this level with the plane of the first rib is not materially altered. The apparent fullness of the supraclavicular fossae and intercostal spaces in emphysema and the increased depth of these hollows in pulmonary tube ulosis

tumor, a single myeloma and giant cell tumor must be considered, and when multiple regions are seen, metastatic malignant disease or multiple myelomas are possible.

Malignant tumors of the sternum may arise in the sternum and its neighboring cartilage. They grow posteriorly, encroaching on the anterior mediastinum. Likewise tumors may arise from the spinal column and its surrounding structures and extend anteriorly and encroach on the posterior mediastinum They may extend laterally, displacing the lung and pleura and occupying the apical or other thoracic regions. At first, from either point of origin, these tumors remain circumscribed. Later they extend through their own capsule and invade or surround the mediastinal structures. These tumors may extend to the pleura and lungs, and may metastasize to the lungs, liver, spleen, kidneys and other organs.

The symptoms of malignant tumors of the sternum are pain, cough, dyspnea, tumefaction and mediastinal pressure These symptoms develop and progress more slowly than when lymphosarcomas are present in the mediastinum and producing similar symptoms.

Physical examination may reveal a mass near the site of origin, especially if the tumor arises from the sternum or its cartilaginous attachments. Any or all of the physical signs of mediastinal tumors with compression phenomena may be elicited.

Both anteroposterior and lateral roentgenograms are useful in demonstrating the size and situation of the tumor At times the roentgenographic study may be helpful in establishing the nature and origin of the growth The presence of hemorrhagic pleural fluid may indicate the presence of malignancy in the thoracic cavity.

Surgical removal, in the early stages, is the preferred treatment.

SYMPTOMS OF RESPIRATORY DISEASE

The symptoms often significant of pulmonary disease are pain in the chest, cough, expectoration, hemoptysis, cyanosis, dyspnea, stridor and hoarseness.

Pain in the Chest Pulmonary tissue and the visceral pleura are devoid of the sense of pain The parietal pleura is richly supplied with sensory nerves from the intercostals Stimulation or irritation of the parietal pleura produces a sharp pain which can be located with fair accuracy over or near the point of stimulation. The diaphragmatic pleura is also sensitive, but stimulation of it never produces local pain, the pain is always referred The central part of the diaphragm is innervated by the phrenic nerve, and the afferents from here enter mainly the third and fourth cervical posterior nerve roots; the peripheral part of the diaphragm is innervated by the lower intercostals, and the afferents enter the seventh to twelfth posterior nerve roots Pain, therefore, from the central portion of the diaphragm is referred to the neck and the upper part of the shoulder, from the outer parts of the diaphragm it is referred to the lower part of the thorax, lumbar region and abdomen The stronger the pleural stimulation the wider is the area of the referred pain, and it may even extend to the other side of the body.

There are many types of pain which may be felt in or about the thorax, all of which are commoner than those arising in the pleurae and lungs For instance, there are muscular pains due to strain or even tearing of muscle fibers; the boring pain of an eroding aneurysm; root pains attending tabes dorsalis, syphilitic meningitis, tumors of the cord, herpes zoster, spondylitis and other lesions which involve the posterior nerve roots, the substernal pain on swallowing which may be associated with esophageal obstruction. There are the pains of angina pectoris and aortitis Pains in the breast may be considered to be pains in the chest. Referred pains from perforating peptic ulcers are by no means uncommon. The pains of true intercostal neuritis are common, but difficult to diagnose.

is about opposite the sixth cartilage and rib from the sternum to the mammary line, opposite the eighth in the midaxillary line, the tenth in the scapular line, and the eleventh near the vertebrae. The lowest part of the lung is on the side at the midaxillary line or a little posterior to this, but the line from here posteriorly, although rising slightly, is nearly horizontal

THE FISSURES AND LOBES OF THE LUNGS The left lung has one fissure and two lobes, an upper and a lower The right lung has two fissures and three lobes, an upper, a middle and a lower (Fig. 9-2).

The relations of the fissures to the surface are variable. They generally appear posteriorly at different levels, the right main fissure being lower than the left. The fissure of the left lung appears at the side of the vertebral column at a variable point extending from the third rib to the upper border of the fifth rib. In the axillary line it is at the fifth rib, although it may be slightly higher or lower, and it ends beneath the sixth rib or the interspace above or below, anywhere from 2⅖ to 4⅓ inches (about 6 to 11 cm) from the midline

The main fissure of the right lung leaves the vertebral column opposite the fifth rib or at the root of the spine of the scapula. The fissure tends to follow the fifth rib, being beneath the rib or beneath its interspace in the midaxillary line and ending at the sixth rib in the mammary line

The subsidiary fissure of the right lung leaves the main fissure in the posterior axillary line opposite the fifth rib and running horizontally forward ends near the sternum at any point between the third and fourth interspaces.

Diseases of the Thoracic Wall. The diseases of the thoracic wall are usually secondary to those primarily affecting the skin and subcutaneous tissues, muscles, bones and nerves, or to diseases originating from the structures within the thoracic cage

Tumors of the Thoracic Wall. Both benign and malignant tumors occur in the thoracic wall. Lipomas are of common occurrence over the shoulders and back and in the axilla. Likewise fibromas occur in the same situations. Cysts may arise from the cutaneous glands over the back. Pigmented nevi in aging persons are of common occurrence over the back

The primary malignant tumors of the thoracic wall arise in the skin, subcutaneous tissues, the breast and the bony framework. The malignant tumors of the *skin* are those common to glabrous skin. They are carcinomas and melanoepitheliomas Carcinomas when present are often situated over the shoulders and scapular regions, originating in sebaceous glands which abound here The tumors of the soft tissues which undergo malignant change are fibromas and hemangiomas These tumors are described in the section on diseases of the skin. A common malignant tumor of the thoracic wall is carcinoma of the breast The tumors which originate in the *bony framework* are multiple myelomas, Ewing's tumors of the ribs, osteogenic growths and chondrosarcomas, all of which are rare and are considered in this text with tumors of the bones

Metastatic tumors of the ribs are frequent. They may be clinically silent, causing no symptoms, or at times they may be the first manifestation of malignant disease when a pathologic fracture occurs. Malignant tumors of the breast, prostate gland and thyroid gland, and hypernephromas are especially likely to cause metastasis to the ribs and spinal column. Cancer of the breast in women and cancer of the prostate in men are most likely to cause pathologic fracture of the ribs

The symptoms of metastatic tumors of the ribs are dull aching pain and, most frequently, intercostal neuralgia. When the lesion is in the upper ribs, the pain often has a brachial plexus distribution. The patient may discover a swollen or tender region which persists.

Often the results of examination are negative if there are no fractures present. Examination by physical means *is never diagnostic of rib tumors.* Diagnosis *is* established by roentgenographic examination. When the tumor is su[illegible]'s

blood from the stomach, *hematemesis*. The bloody sputum of hemoptysis is bright red, contains froth and does not contain food. When in doubt about whether there has been hemoptysis or hematemesis, ask the patient whether the blood came from the lungs or the stomach The patient can often answer this question correctly and may even state correctly the side of the chest from which the hemoptysis came

When blood is intimately mixed with mucus in the sputum, the color varies according to the relative quantities of these two constituents and the length of time after they have been mixed. Thus, in pneumonia, the sputum may have a brick-dust tint (rusty sputum), or it may be outspokenly hemorrhagic Mucohemorrhagic sputum is also met with in hemorrhagic infarction of the lung and in neoplasm.

The so-called prune juice sputum (an unnecessary term) is a serohemorrhagic sputum. It is met with when a croupous pneumonia is complicated by edema of the lung A peculiar mucohemorrhagic sputum of sticky consistency, said to resemble currant jelly (another unnecessary connotation) has been described in those who have neoplasm and sometimes in pulmonary syphilis

Small streaks of bright blood in sputum otherwise of mucous character usually originate in the upper air passages or in the mouth

Blood-stained saliva is often brought to the physician by the hysterical and by simpletons It is usually a thin fluid, of stale odor and of brownish red color.

Color of the Sputum Sputum may be of different colors, owing to the admixture of various coloring matters *Black sputum* is seen in coal-miners and iron-workers; *blue sputum* is occasionally seen in workers in dye works, *green sputum* is met with in pneumonia with jaundice, sometimes in caseous pneumonia, and occasionally in pyocyaneus infections, *yellow sputum* may be due to hematoidin in pulmonary abscesses, or to bile when hepatic abscesses break into the lung In chronic passive congestion of the lung in cardiac disease, a *yellowish red* tint may appear, owing to the large number of pigment-containing cells—heart-failure cells—in the sputum.

Odor of the Sputum Usually stale, the odor of sputum may become putrid from decomposition in the mouth or in the air passages (fetid bronchitis, bronchiectasis, pulmonary gangrene) There is no odor more sickening than that of fetid sputum

Consistency of the Sputum The consistency of sputum depends on the relative amount of mucus it contains, in asthma, and sometimes in pneumonia, the sputum is so tenacious that it must be wiped from the mouth.

Protein Content of the Sputum. Sputum arising chiefly from increased secretion of the bronchial mucous membrane, as in asthma and in bronchitis, is poor in protein, whereas sputum arising in inflammations of the lung substance itself, for instance, or in transudations, such as pulmonary edema and chronic passive congestion, is rich in protein. The protein loss in the sputum, except in hemoptysis, is not of sufficient quantity to be of practical importance The urea content of the sputum closely parallels the concentration of urea in the blood

Particulate Matter in the Sputum Fragments, occasionally pieces of pulmonary tissue, may be coughed up in gangrene or in pulmonary abscess Pieces of *tumor* and *tumor cells* often appear in the sputum The finding and identification of tumor cells in the sputum are valuable diagnostically and these are searched for in all instances of suspected malignant disease of the lungs or bronchi

Sometimes branched fibrinous casts of the bronchi are coughed up in fibrinous bronchitis, in croupous pneumonia or in diphtheria. These are recognizable with the unaided eye They are of no particular diagnostic significance. When they are small, if desired these casts may be isolated by shaking the sputum with water.

Curschmann's spirals, Charcot-Leyden crystals, tuberculous lenses, and Dittrich's plugs are terms which are the remnants of former days and convey no implications of definite pathologic significance In the decomposing sputum of putrid bronchitis, of bronchiectasis, and of pulmonary gangrene, small yellowish white masses may be present

COUGH A cough consists of a forcible, explosive expiration during which the glottis is first closed and then quickly opened. The current of air passing between the vocal cords gives rise to a noise that is at first of high pitch, becoming lower as the glottis opens.

A cough is a defensive mechanism which, when properly used, helps to cleanse the larynx, the trachea and the larger bronchi. The sensory stimulus passes up the vagus to the cough "center" in the medulla oblongata which lies close to the respiratory center.

Unnecessary coughing injures the mucous membranes of the air passages. Violent coughing can injure the elasticity of the lung, especially in its upper parts Coughing exerts an important influence on the circulation. As results of coughing, the intrathoracic pressure is increased, the inflow of venous blood is hindered, and the outflow of arterial blood is favored, so that the arterial pressure may momentarily be increased. This sudden heightening of the blood presure may lead to arterial rupture in atherosclerosis or in aortic aneurysm, it accounts for the conjunctival hemorrhages in any patient who has a violent cough. Prolonged violent coughing may cause extreme soreness and tenderness in the epigastric muscles.

When nothing is expectorated, the cough is dry or empty, as in cutaneous or in pleural irritation.

A hacking or frequently recurring feeble cough indicates continuous slight irritation, it is met with in acute and chronic catarrh of the upper air passages. Violent paroxysms of coughing, difficult to allay, are common in convalescence from influenza. The so-called goose cough or brassy cough of aortic aneurysm is characteristic only of a mediastinal tumor with pressure on the recurrent laryngeal nerve. The whoop of whooping cough has only to be heard once to be afterward easily recognizable However, the whoop is not limited to whooping cough It occurs in any severe irritating cough in either children or adults There is a laryngitis caused by Pfeiffer's organism occurring in adults which often is accompanied by the whoop. These affections are often termed second attacks of whooping cough

In summary it is well to repeat Pottenger's definition of the mechanisms of cough, which consist of (1) a sensory disturbance in the larynx through the superior laryngeal nerves, (2) a closure of the glottis through the superior and inferior laryngeal nerves, (3) a contraction of the expiratory muscles (internal intercostals and abdominal) through the thoracic spinal nerves, and (4) relaxation of the inspiratory muscles (diaphragm, external intercostals, intercartilaginous muscles of the shoulder girdle) through the cervical and thoracic spinal nerves

THE SPUTUM. The sputum expectorated on hawking or coughing consists of a mixture of secretions from the mucous membranes with pus, blood or other materials given off from the respiratory apparatus The secretions come from the mucous membranes of the larynx, trachea and bronchi, pharynx and back of the nose. In addition to these secretions, the sputum contains saliva, secretions from the mucous membranes of the mouth, and food particles

The amount of sputum is extremely variable and depends on the disease process present The largest amounts are met with in certain bronchial affections; in large bronchiectatic or phthisical cavities, in pulmonary edema; or when abscesses or empyemas break into the bronchi. In such cases the sputum may be brought up in mouthfuls (as much as 1 to 2 liters daily).

Varieties of sputum are designated according to the predominating constituent present. Four main varieties of sputum are described: mucous, purulent, serous and bloody. Other forms of sputum are admixtures of these, for example, mucopurulent, and mucohemorrhagic.

Sometimes there is expectoration of pure blood, which is termed *hemoptysis*. In hemoptysis, the blood is coughed up; it is distinguished from the vomiting of

whether from primary heart failure or from heart failure secondary to fibrosis of the lungs and the pneumoconioses, emphysema, or arteriosclerosis

Deficient aeration of the blood such as occurs in tracheal obstruction, bronchial asthma, uncomplicated emphysema and in the acidosis of uremia or diabetes is an important cause of dyspnea. The dyspnea thus produced is enhanced by myocardial insufficiency with an ensuing degree of pulmonary congestion. In pulmonary congestion the lungs become stiffened and less distensible, and therefore a reflex, mechanical factor of dyspnea is added

Dyspnea may also occur as a hysterical manifestation, either in the form of attacks of deep sighing respirations, usually following some emotional disturbance, or occasionally even as paroxysms of hyperpnea, with deep and labored breathing. If the resulting hyperventilation persists long enough, alkalosis with tetany ensues

Certain clinical varieties of dyspnea associated with certain phases of respiration are commonly recognized Inspiratory dyspnea is due to obstruction of the larynx or trachea which slows the respiratory rhythm by prolonging and deepening inspiration; it causes apprehension and often anguish to the sufferer, and is accompanied by a collapse, during inspiration, of the soft parts above the sternum and below and between the ribs

Expiratory dyspnea is due either to an advanced loss of pulmonary elasticity, as in emphysema, or to generalized bronchial spasm, as in asthma. Dyspnea of effort is a symptom of many types of respiratory disease. It is a principal sign of the disturbances of pulmonary circulation caused by cardiovascular diseases.

Orthopnea in Pulmonary Disease. Orthopnea is dyspnea present even when the patient sits up It represents a serious exhaustion of the respiratory reserve which consists of an urgent need for oxygen and an accumulation of carbon dioxide in the blood Compensation is striven for by an increased depth of respiration; this is obtained by prolonging and deepening respiration, with little or no increase in rate Orthopnea attends laryngeal and tracheal obstruction, the diffuse bronchial spasm of asthma, and the diffuse spasmodic obstruction of the earliest stage of bronchiolitis. In all conditions attended by an increased rigidity of the lungs, for instance, in the pneumonias, in massive collapse of the lung, in all forms of pulmonary congestion or edema, and in diffuse miliary tuberculosis breathing is shallow and rapid

STRIDOR. Air passing in and out of a partially obstructed larynx or trachea may produce a harsh, vibrating noise This vibrating noise is termed stridor. It is a noise produced in the larger air passages in the same way that rhonchi are produced in the smaller ones Stridor may occur during any part of the respiratory cycle It is ordinarily most obvious in inspiration and during coughing, imparting a harsh, high-pitched quality to the cough The obstruction of the larynx and trachea may be intrinsic, as, for example, by a diphtheritic membrane, or it may be extrinsic, as, for example, a mediastinal tumor, or from kinking of a bronchus such as may be produced by localized fibrosis of the lung. The obstruction of a main bronchus is attended by a wheeze, not stridor

HOARSENESS In disease inside the thorax the larynx is often secondarily affected, either by local inflammation or by paralysis due to pressure on the recurrent laryngeal nerve The dysphonia which ensues may vary from a mild huskiness to aphonia. The extent of the loss of voice is not a measure of the seriousness of the lesion.

Acute laryngitis causes a dysphonia which passes off as the inflammation resolves The voice may be altered by extrinsic factors also—nasal obstruction, tracheal obstruction, pharyngitis, and chronic disease of the lungs Aphonia or soft whisper may occur in neurotic patients.

Hoarseness which persists in persons more than 40 years old may be due to a tumor of the larynx, either benign or malignant

They consist of particles of tissue or of small masses of pus which have undergone decomposition in the lungs or in the bronchi Sputa containing these materials have a foul, fetid odor.

Small, soft, yellowish white particles consisting of fungi are common in pulmonary tuberculosis and in chronic bronchitis. In actinomycosis of the lungs these particles are termed sulfur bodies. Pulmonary stones may be present in sputum, and when the patient inquires about them a correct answer should be given These stones are portions of calcified lymph nodes.

CYANOSIS IN PULMONARY DISEASE. The blue color of the skin and mucous membranes in cyanosis is due to the presence of sufficient reduced hemoglobin in the capillaries to give the color which shows through the skin A minimal content of 5 gm of reduced hemoglobin per 100 ml. of blood is necessary before the blue color is apparent In profound anemia, however, with a hemoglobin content of less than 5 gm., the amount of reduced hemoglobin cannot reach this minimal content, even in the presence of marked anoxia, and thus the profoundly anemic patient will not be cyanosed. The greater the amount of reduced hemoglobin, the deeper the cyanosis. It is best seen in the lips, nose, cheeks, ears, fingers and toes It can be temporarily abolished by pressing out the blood from the part. The intensity of the color depends also on whether the small peripheral vessels are dilated or contracted.

The blood in the capillary vessels may contain an excess of reduced hemoglobin either because it left the heart in this condition, or because there is an abnormal, excessive change of oxyhemoglobin to reduced hemoglobin while the blood is passing through the peripheral capillary system

Abnormally slow passage of the blood through the peripheral capillaries allows the tissues to take more oxygen from it than usual, and so to produce more reduced hemoglobin Slowing of the peripheral circulation is a normal response to cold, and mild degrees of local blueness are compatible with good health. When capillary stasis or poor blood flow is associated either with general circulatory failure or with some form of local vascular paralysis it is indicative of serious disease.

It is not always easy to determine the cause of cyanosis in a particular patient, whether it is respiratory or circulatory or a combination of both. When the capillaries are engorged, the pulse full, the flow rapid, there is in addition to the deficient oxygenation in the lungs an associated carbon dioxide retention, with peripheral *vasodilatation and an inadequate circulation In some instances* of inadequate circulation the cyanosis is deep and florid, and the patient breathes heavily, while in others the skin may be pale, cold and wet, with leaden livid cyanosis, indicating poorly filled capillaries in a patient who has respiratory and circulatory failure, a rapid feeble pulse and quick, shallow breathing

Cyanosis may also result from the formation in the blood of certain derivatives of hemoglobin Methemoglobin is produced by large doses of drugs such as chlorates, coal-tar derivatives and sulfonamides These drugs may also determine the formation of sulfmethemoglobin, which gives rise to a leaden type of cyanosis.

DYSPNEA IN PULMONARY DISEASE. Dyspnea is characterized by difficult, painful or disordered breathing. Hyperpnea is increased breathing. A healthy person *is not conscious of any increase in respiration until the normal rate is doubled.*

The obvious causes of dyspnea are many, for instance the various diseases of the lungs and pleura, cardiac failure, anemia, the acidosis of uremia or diabetes, increased intracranial pressure and hysteria. The important causes are: chemical alterations in the blood flowing through the respiratory center, and local conditions in the lungs which make them more rigid and less easily distensible and cause rapid and shallow breathing. Rigidity or decreased distensibility of the lungs is by far the more usual factor in the dyspnea. It determines the dyspnea of pneumonia, of pulmonary edema and of massive collapse of the lungs. Pulmonary congestion, with consequent rigidity of the pulmonary tissue, is the cause of cardiac dyspnea,

whether from primary heart failure or from heart failure secondary to fibrosis of the lungs and the pneumoconioses, emphysema, or arteriosclerosis.

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EXAMINATION OF THE LUNGS AND PLEURAE

In studying clinically the condition of the lungs and pleurae, the physician employs the aids of inspection, palpation, mensuration, percussion, auscultation and exploratory puncture The roentgenologic examination of the lungs and pleurae, often aided by the intrabronchial use of radiopaque substances, is more precise and reliable than any other examination by physical means. The bronchoscopic examination is more precise for the purposes of diagnosis in certain instances than any other examination

The Respiratory Movements. The lungs make no active movements of their own during respiration, but simply follow passively the movements of the wall of the thorax and of the diaphragm Two main types of inspiratory expansion of the thorax are seen In the *costo-abdominal* type the expansion is due chiefly to the descent of the diaphragm, and less to the elevation of the ribs In the *costal* type the opposite is the case, the expansion being due chiefly to elevation of the ribs

The diminution in size of the thorax during expiration depends normally on the elasticity of the lungs and ribs, *not on muscular contraction.*

The times occupied by inspiration and expiration, respectively, are approximately equal, and there is no pause between the two.

FREQUENCY AND RHYTHM OF THE RESPIRATIONS. The number of breaths taken by healthy adults varies between 16 and 20 per minute. The rate in disease may be increased or decreased.

Increase of the frequency of respiration (dyspnea or tachypnea) is met with in most diseases of the respiratory system, in many diseases of the heart, and in those diseases of the abdomen that hinder the movements of the diaphragm In dyspnea the number of respirations may reach 40, 60, or more per minute In certain diseases of the nervous system excessive tachypnea may occur in paroxysms

Mechanisms of the production of tachypnea are discussed under Heart Disease (Chapter 10)

Slowing of the respiration (bradypnea) may be met with in affections of the brain or of its membranes, in irritations of the respiratory center in the medulla; in severe infections and in uremia.

Cheyne-Stokes Breathing. In this form of respiration, periods of complete cessation of the respiratory movements alternate with periods in which the respirations slowly increase in frequency and volume to a maximum, and then again decrease until they cease

The phenomenon is met with in many normal persons while asleep and therefore is inconsequential in illness despite the fact that it is observed in an *exaggerated* form in many patients who are seriously or critically ill During the apneic phase these very ill patients are sleepy, and the pupils are contracted and nonreactive; as the respiratory movements return, the psyche awakens, and the pupils dilate and again become responsive

In *Biot's breathing* the respiratory pauses are long (from 5 to 30 seconds or more), in periods which may recur more or less regularly or wholly irregularly

Dyspnea is observed normally on exercise and in disease either of the lungs or of the circulatory apparatus As dyspnea increases, the patient sits up in bed, with his head, arms and thorax held rigid, panting for breath; and the *condition is* then termed orthopnea.

DETERMINATION OF THE VOLUME OF THE INSPIRED AIR AND OF THE EXPIRED AIR (SPIROMETRY). The measurement of the air entering and leaving the lungs in each phase of respiration can be made by means of a spirometer.

Certain terms which have been established in spirometry should be understood, since these terms may be employed in description of minute output of the heart determined by gasometric methods (carbon monoxide), and occasionally on patients

who have heart disease. By *vital capacity* is meant the amount of air that, after the deepest possible inspiration, can be expelled on full expiration; in healthy men it varies from 3,000 to 4,000 ml ; in women it varies between 2,000 and 3,000 ml The vital capacity is smaller in old age, as well as in all diseases of the respiratory system

Tests of pulmonary function offer a method of appraising pulmonary disabilities objectively. They are of value in determining the absence of pathologic alterations in some of the nonpulmonary types of dyspnea, as seen in neurocirculatory asthenia and hysteria; the course of various pulmonary diseases can be followed objectively; and the preoperative use of the tests will indicate fairly accurately the results of such surgical procedures as collapse therapy, lobectomy, and pneumonectomy

The increased interest in pulmonary physiology since surgical operations on the lungs and the heart have become commoner has brought about a revision of the terminology used to describe the various components of respiration.

Inspiratory Reserve (Complemental Air). This measures the maximal amount of air which can be drawn into the lungs, using the resting expiratory level as the starting point. Normally this amounts to 3,000 ml.

Expiratory Reserve (Supplemental Air) This measures the maximal amount of air which can be expired, using the resting expiratory level as the starting point Normally this amounts to 1,000 ml

Residual Air (Residual Capacity) This represents the air remaining in the lungs following a maximal expiratory effort This quantity cannot be measured spirographically and its determination depends on measuring the amount of nitrogen displaced by breathing 100 per cent oxygen

Functional Residual Capacity This represents the quantity of air remaining in the lungs after the completion of a quiet respiration It is the sum of the residual air and the expiratory reserve

Maximal Breathing Capacity This is a measure of the maximal volume of air that can be breathed in a unit of time The maximal breathing capacity differs from the vital capacity in that it expresses a time relationship The same information can be obtained by measuring the vital capacity and relating it to the time required for expiration.

The amount of air taken in during a minute of quiet respiration varies from 5 to 7 liters

The vital capacity of the lungs enlarges on bodily exercise and in pathologic states accompanied by dyspnea.

INTERCOSTAL RETRACTION AND EXPANSION On inspection of the thorax it is well to observe the rate of the respirations and record it. The progression of expansion of the lungs is followed during inspiration with particular reference to the lack of filling and consequent expansion in any part of the lung and especially at the apices In the adult in a normal state of nutrition there is no noticeable expansion or retraction in the intercostal spaces.

The Diaphragmatic Phenomenon (Litten's Sign). In emaciated adults the respiratory movements of the lower margin of the lungs can sometimes be observed as a furrow, descending during inspiration over the intercostal spaces, especially in the lower part of the right side of the thorax (Litten's sign) This is due to the separation of the diaphragm from the thoracic wall when it contracts; before the lungs can follc [illegible]

adh[illegible]
formation

Mensuration of the Thorax. By passing a tape around the thorax, just above the nipples, the patient's arms being held out from the sides, the circumference of the thorax is measured On physical examinations for entrance to the army or navy, and for life insurance, this value is used as a measure of the development of

the thorax, and serves as a clue to the general constitution of the person. In healthy young men the circumference should exceed 32 inches (about 81 cm).

More important as regards the state of the lungs themselves is *the difference in circumference on deep inspiration and on deep expiration.* Normally this difference amounts to about 2⅘ inches (7 cm.) or more

The comparison of the *circumference of each of the two halves* of the thorax shows normally a difference of from 0 5 cm. to 2 5 cm. in favor of the right side In an asymmetric thorax, owing to unilateral expansion or retraction slight differences in circumference of the two halves of the chest can be easily recognized

Exact records of the form of the thorax are made with a *cyrtometer.*

Palpation of the Thorax Over the Lungs and Pleurae. A part of the palpation of the thorax is the testing of the vocal fremitus, the vibration of the voice propagated to the thoracic wall through the bronchi and pulmonary tissue. The test is made by placing the two hands on symmetric portions of the thoracic wall and asking the patient to repeat in a deep voice "1, 2, 3," or "99." In health the vocal fremitus perhaps is more marked on the right than on the left side In women the vocal fremitus is weaker than in men. Vocal fremitus sometimes is helpful in deciding whether dullness over the lower part of the thorax is due to infiltration of the lung or to pleural effusion; increased vocal fremitus indicates better conduction from the larynx to the lung surface (infiltration), while enfeeblement or abolition of the fremitus suggests pleural effusion or pneumothorax. However, in massive pneumonia, with plugging of the bronchus, the propagation of the voice may be temporarily interfered with, again, in pleural effusion, there may be less diminution of the vocal fremitus than might be expected because pleural adhesions, uniting the lung to the wall of the thorax, may favor the conduction of the voice tremor, or an atelectasis, due to the pressure of the exudate, may increase the vocal fremitus more than the effusion weakens it

Percussion Over the Lungs and Pleurae. In percussion a shock is given by the percussion stroke which gives rise to sounds that vary with the elasticity (capacity for vibration) of the parts struck; the greater the elasticity, the more marked is the production of sound

PRINCIPLES OF PERCUSSION. Airless bodies enter into sound-producing vibration only when they are rigid or in a certain state of tension. In the human body, bones alone correspond to such a state

The sounds yielded by soft parts when percussed depend on the air or gas content If the air or gas is contained in large cavities, it is set into vibration, and along with it the wall of the cavity is started vibrating; if the air is distributed and confined throughout the whole tissue, as in the lungs, the air and the tissue vibrate together on percussion. Percussion then permits of an approximate delineation of the limits of juxtaposed airless and air-containing structures.

DIRECT PERCUSSION. The fingers are arranged in a plane with the middle finger stiffened and slightly flexed toward the palm and, to produce the sounds, deliver the



Fig 9-4 Direct percussion employing the stiffened *middle finger*



Fig 9-5 Direct percussion with the end of the middle *finger.*

stroke directly on the surface of the thorax, with the middle finger, without any intermediary plessimeter (Fig. 9-4). A better method is to use the end of the finger as in Figure 9-5.

INDIRECT PERCUSSION. In this method, the blow, instead of being struck directly on the body surface, is delivered on some intermediate body placed upon the part under study. This intermediate body is called a plessimeter or pleximeter. As a *plessimeter* the middle finger, called a plessimeter finger, is used (Fig. 9-6) To ascertain the condition of the structures behind the clavicle, the clavicle itself often is used as a plessimeter.



Fig 9-6. Indirect percussion employing the middle finger as a plessimeter

The plessimeter finger is most often used because it permits judgment of the feeling of resistance, thus yielding some information accessory to the percussion sounds. It is easy to approximate the finger to the surface such as the intercostal spaces and supraclavicular fossae.

As a *percussor*, or *plessor*, it is customary to use the middle finger of the right hand, flexed to an obtuse angle at the two distal terminal joints, and slightly flexed at the proximal joint of the finger (Fig 9-6). The stroke is delivered entirely from the wrist, the forearm remaining in position. With practice one soon learns how best to deliver the stroke. As a rule, the percussing finger should be allowed to rebound immediately from the plessimeter after it has struck, in order that the plessimeter may freely vibrate with the part beneath. In gentle percussion the plessimeter finger should lie in smooth contact with the part under study; for deep percussion it may be firmly pressed against this part.

In *orthopercussion* the force of the blow is directed exactly perpendicular to the surface

The *strength of the percussion stroke* should vary greatly according to the conditions of the examination. When the soft parts over the organ under examination are thick, the stroke must, of course, be harder to set that organ in vibration

In the determination of so-called *deep or relative dullness* of the heart, however, it is necessary to use a somewhat stronger stroke, though even here ones does best to use percussion of medium force rather than the very strong percussion so often employed

THE INTENSITY AND QUALITY OF THE SOUNDS PRODUCED ON PERCUSSION. In percussion of the thorax, as elsewhere, attention is directed, regarding the sounds produced, to their *loudness*, their *pitch*, and their *clang* or *timbre*.

Comparative Percussion of the Lungs. In health the pulmonary resonance on percussion varies somewhat over different regions of the thorax, corresponding to the variable thickness of the soft parts and to the variable volume of lung beneath. In some places the sound is louder and fuller than in others. By repeated percussion of the healthy chests of different persons there gradually become fixed in mind memories of the normal sounds heard, and of the normal resistance felt, on percussion over the lungs It is learned how much muffling, or dulling, of the sound may be due to varying degrees of obesity and to different degrees of muscular development The percussion sound is always clearer in front and at the sides than behind. In fat persons the resonance on percussion over the back may be impossible to evaluate.

It is always well to compare the percussion sounds yielded by symmetric parts

on the two sides of the chest, beginning with percussion of the supraclavicular fossae above and passing downward on the two sides over the several intercostal spaces, making sure to percuss always with the same force and to direct the stroke in the same way.

The breathing should be quiet and normal during percussion. The loudest sounds are normally met with between the third and the fifth ribs in front.

It is wasted time to percuss over the tympanitic space of Traube (fourth to sixth rib on), owing to the presence of the stomach under the left side and front of the lower part of the thorax In comparative percussion of the two sides of the chest, asymmetries of the two sides of the thoracic wall are important. A slight grade of scoliosis may affect the sounds.

The loudness of the percussion sounds depends, essentially, on the amount of air or gas in the organ examined.

The terms clear and dull refer to the *intensity* of the sound Clear and dull are used, clinically, *in a different sense from that of ordinary speech. Clinically, reference to the* loudness of sound is to the amplitude of the sound waves that strike the ear drum. This intensity depends on the capacity for vibration and the strength of the percussion blow. In comparative percussion, therefore, use exactly the same force, and avoid confirming a preconceived opinion by unequal force of the percussion blows, for unequal force will produce unequal sounds and dullness may thus be simulated

The *pitch* of a tone depends on the number of vibrations per second The greater the number of vibrations, the higher the tone Percussion sounds are always *noises,* composed of a large number of individual *tones.* The lowest tones are met with over the distended lungs in pulmonary emphysema A percussion sound, therefore, that contains very low tones is usually loud, clear and full.

The ear should be carefully exercised in the appreciation of the lower tones on percussion When one tone is dominant, as in tympanitic sounds, the height of its pitch is easily recognizable to one who has a good tone-pitch sense. The recognition of differences in the pitch of the dominant tone in tympanitic sounds lies at the basis of the recognition of alterations in pitch.

In general it may be said that a *tympanitic sound* over a lung, except in Traube's space, which is situated in the lower part of the left lung, indicates an abnormal condition within the thorax such as pulmonary cavities, bronchiectatic cavities, abdominal viscera dislocated into the thorax, or a change in the structure of the lung that leads to loss of the tension of the alveolar walls, for example, atelectasis of the lung, from bronchial occlusion, or from compression due to high position of the diaphragm, large pericardial effusions, or pleural effusions, or in edema of the lung, in certain stages of pneumonia when the alveolar septa have changed in texture from the inflammation, though the air content is not yet essentially diminished, or in bronchial pneumonia, in which the bronchi in airless tissue may give rise to a tympanitic note

A *metallic* or *amphoric sound* on percussion depends on the presence of high overtones accompanying and obscuring a low fundamental tone It arises in large gas-containing cavities with tense walls. It will appear in the blown-up stomach if the distention is sufficiently increased. To grow familiar with this sound, it may be elicited by thumping over the cheek after the mouth has been so strongly distended by air that the tympanitic sound, present on less distention, disappears

A *cracked-pot sound* (or metallic clink) arises, on strong percussion, if air or gas is thereby driven out of a cavity through a narrow opening

THE FEELING OF RESISTANCE ON PERCUSSION It may be possible to draw more precise conclusions from percussion if the examiner not only listens, but feels with the finger which is being percussed The sense of resistance *felt by the fingers* on percussion varies with the compressibility of the part percussed. It is readily admitted that percussion areas do not correspond to anatomic projections, but by practice of finding these areas in the normal thorax, pathologic changes can often be recognized and the clinician is better for having this experience.

The Upper Limits of the Pulmonary Resonance on Percussion. Normally the upper limits are in the same position on the two sides. On each side the limit extends for a distance of from 1⅕ to 1⅗ inches (about 3 to 4 cm) above the clavicle at the level of the spine of the sixth or seventh cervical vertebra, and, behind, goes over the edge of the trapezius muscle obliquely downward and mediad into the posterior medial pulmonary limit at the level of the spine of the second thoracic vertebra (Krönig's fields of pulmonary resonance at the apices).

Normally the upper margin of the lung reaches a point, above the clavicle, corresponding to the position of the tubercle on the first rib, which can be felt on palpation between the heads of the sternocleidomastoid muscle

The Lower Limits of the Pulmonary Resonance on Percussion. These can be approximately determined by percussion

The lower limit of the pulmonary resonance varies with the phases of respiration and with the position of the patient On forced inspiration the boundaries may descend ⅘ to 1⅕ inches (about 2 to 3 cm) below the level found in quiet breathing In the dorsal decubitus the lower margin is ⅖ to ⅘ inch (about 1 to 2 cm.) below its position in the sitting posture, in the lateral decubitus, that of the upper lung may descend 1⅕ to 1⅗ inches (about 3 to 4 cm) lower

Abnormal Position of the Boundaries of the Lungs The determination of the pulmonary limits may, in pathologic states, show a general expansion, a displacement only of the lower boundaries, a general contraction, or a displacement of either the lower or the upper limit

General expansion of the pulmonary limits is met with in chronic emphysema and in the temporary inflation of the lungs due to tracheal or laryngeal stenosis, diffuse bronchitis and bronchiolitis, or asthma The lower limit may be lower than normal from compensatory emphysema of the lower part of the lung when the upper part is diseased, for example in apical tuberculosis, or when the opposite lung is diseased

General contraction of the pulmonary limits is met with when the total amount of air-containing tissue in the lungs is diminished from any cause, that is, prevention of entrance of air into the lung or compression of the lung from thoracic tumors or abdominal distention

The *lower limit of a lung may be higher* than normal when the diaphragm is high, as in abdominal distention or in retraction of a lung, or when parts of the lung are deprived of air, as in bronchostenosis A very common cause for displacement of the lower limit of pulmonary resonance upward is the accumulation of fluid in the pleural cavities When the pleura is nonadherent, the fluid tends to accumulate chiefly in the lateral parts, the line of the dullness does not, as a rule, run horizontally, but in a curve, the highest point of which lies approximately in the posterior axillary line, descending rather abruptly in front, and more gradually behind (S-shaped line of Gardner)

Retraction of the upper limit is most often due to pulmonary tuberculosis The retraction of the apex is usually first demonstrable at the upper medial margin in front

DULLNESS AND FLATNESS ON PERCUSSION. The percussion sound is dull in all conditions in which the air content of the lung percussed is less than normal

When the lung is separated from the thoracic wall by fluid, there must be at least 500 ml to yield dullness on percussion An immediate change of the dullness with change of position indicates the simultaneous presence of air and fluid

Auscultation of the Lungs. On auscultation of the lungs the examiner listens (with the aid of a stethoscope) to the sounds that accompany inspiration and expiration and the voice sounds that are audible over the thorax. Application of the ear to the thoracic wall is no longer employed unless the stethoscope has been left at home Under these circumstances a great deal of information may be gained.

The voice sounds are better heard with the naked ear than with the aid of a stethoscope, but the breath sounds and, especially, some of the modifications that these undergo in disease, as well as some of the sounds that accompany them, are better recognized and localized by the use of the stethoscope.

From "Current Comment" in the *Journal of the American Medical Association* (Dec 24, 1949), on the auscultatory respiratory murmur the following comment is quoted:

A new appraisal of auscultation, which is based on clinical experience and facts in physics and physiology discovered since Laennec's time, is claimed to show that the respiratory murmur is composed of sound vibrations originating in all component parts of the respiratory mechanism. It is now maintained that the respiratory murmur cannot be caused by air rushing through the larynx and impinging on the bronchial walls and dilating the air cells because the lungs always contain residual air which stops the force of the incoming current and causes the air to enter the finer bronchi and air cells by diffusion The sound vibrations causing the vesicular murmur are said to originate in the respiratory mechanism in the anterior, lateral and lower portions of the thorax, where the air cells predominate, the musculature is light and the bony cage is elastic. That part of the respiratory mechanism which normally causes the bronchial murmur is found in the superior portion of the thorax and is most distinct posteriorly. Here the sound vibrations are produced by the air current, the larger bronchi, a comparatively small amount of pulmonary tissue and air cells, a heavy musculature and the least elastic portion of the bony cage

THE BREATH SOUNDS. The breath sounds present over the alveolar masses of the lung are called *vesicular breathing* The breath sounds present over the larger air tubes during respiration are termed *bronchial breathing.*

In disease states, when there is secretion of excessive mucus, swelling of the bronchial mucous membrane, or fibrinous exudation on the surfaces of the pleurae, certain accessory or *adventitious sounds* arise These sounds are termed rales, crepitation, friction sounds.

The breath sounds normally are loudest just beneath the clavicles. The sounds are feebler over the apices

MODIFICATIONS OF VESICULAR BREATHING. Accentuated vesicular breathing is heard normally in children, and hence is often spoken of as puerile breathing Puerile breathing may be audible until puberty, more often in girls than in boys

Accentuated breathing is heard in the neighborhood of infiltrated regions, especially at the apex, in incipient pulmonary tuberculosis, and in a healthy lung close to a consolidating region, at the beginning of pneumonia.

Sometimes there is *prolongation of the expiratory sound* of vesicular breathing so that this becomes as long as, or even longer than, the inspiratory sound A prolongation of the expiratory part of the vesicular breath sounds often indicates an expiratory dyspnea, such as emphysema, asthma or bronchitis. If the distribution is limited to the base of the right lung, it may indicate the beginning of congestive heart failure

If the inspiratory sound, instead of being continuous, is interrupted so as to consist of two or more parts, the inspiration assumes a jerking or saccadic character; it is *cog-wheel breathing.* Cog-wheel breathing is often met with in persons of feeble musculature, in nervous people, and in children after crying

BRONCHIAL BREATHING. Bronchial breathing is audible in healthy persons over the spinous process of the seventh cervical vertebra, corresponding to the position of the bifurcation of the trachea, and thence downward to the spine of the fifth thoracic vertebra.

The loudness of bronchial breathing is not important. It is the aspirating, hollow or reverberating character of the sound that is peculiar, and it is often well marked when the sounds are weak. The expiratory portion of the sound in tubular breathing

may, and usually does, approach the inspiratory sound in intensity; its duration is great. In some instances, however, expiration is inaudible in tubular breathing.

Pathologic Bronchial Breathing. The solidifications of the lung over which pathologic bronchial breathing becomes audible include (1) infiltrations due to pneumonia, tuberculosis, or hemorrhagic infarction; (2) compression behind pleural exudates and tumors, and (3) atelectasis The solid regions, under ideal conditions, which are seldom present, must be either near the surface or be connected with it by means of a good sound-conducting medium, moreover, the communicating bronchi must be open Cavitation resulting from the destruction of air sacs, over which pathologic bronchial breathing may become audible, includes bronchiectatic cavities, tuberculous cavities, and larger emphysematous cavities. The communicating bronchi must be open, and the cavities must be near the surface, or must communicate with it by sound-conducting media.

MIXED BREATHING OR BRONCHOVESICULAR BREATHING The term mixed breathing or bronchovesicular breathing is used too frequently and perhaps, in some instances, for the purpose of mental hedging.

Over normal lungs or pleuritic exudates, or when loud rales are present, the respiratory murmur may be so feeble that the character of the breath sounds cannot be recognized "Bronchovesicular breathing" simply means the presence of both bronchial and vesicular elements in the breath sounds

ORIGIN OF THE VOICE SOUNDS. In auscultation of the voice sounds two processes are important (1) the production of fundamental tones in the larynx, where the vocal cords of the glottis act like a reed instrument, and (2) the process of articulation, in which the different tones produced in the larynx are modified by changes in shape of the oral cavity, and adjacent cavities, the larynx itself being unable to articulate The oral cavity, in association with the laryngeal and nasal cavities, constitutes a resonating chamber As such, it intensifies that particular tone or overtone of the sound produced in the larynx the wavelength of which corresponds in resonance to the dimensions of the cavity Variations in the shape of the cavity will modify its function as a resonating chamber in that it will vibrate in unison with notes of different wavelengths or pitch Thus, through changes in the resonating chamber, different overtones may be intensified or weakened and corresponding changes in the voice sounds produced In whispering there is articulation of the breath sounds only, the glottis being passive and giving rise to no loud tones

When auscultation is made over the healthy lungs of a person pronouncing the number "99" in a voice of low pitch, the audible voice sounds are nearly everywhere weak and muffled instead of being loud and clear like those audible over the larynx. When loud, clear voice sounds are audible directly over the bronchi of the healthy thorax, the condition is known as bronchophony The term bronchophony includes all such sounds audible in health and all degrees of clearness greater than this in disease

If it is observed that the sounds have become less clear than formerly, especially if they suddenly disappear over an area, occlusion of the bronchi is often the cause of the disappearance of the sounds

Increased clearness or distinctness of the voice sounds is termed pathologic bronchophony. This term is applied when sounds as clear as, or clearer than, those heard over the upper thoracic part of the spinal column in health are met with in any other part of the thorax. The phenomenon is due either to increased conducting power or to increased reflecting power of the lung tissue The conducting power of the spongy structure of the lung is increased by any change that makes the pulmonary structure more homogeneous

Whispered bronchophony is sometimes clearer than that of the spoken voice. The terms pectoriloquy and whispered pectoriloquy are sometimes applied when the sounds are very clear, apparently close to the ear, and exactly circumscribed.

A special kind of definite bronchophony known as egophony is sometimes heard above the level of the fluid in large pleural effusions that cause partial compression

and narrowing of the bronchi. The voice sounds have a definite nasal quality which is rhythmically intensified and interrupted.

Over large cavities containing air, and especially over a pneumothorax, the voice sounds may have an amphoric, metallic, ringing quality.

Auscultation of the voice sounds yields information comparable in large part to that afforded by palpation of the vocal fremitus; when the voice is not strong enough or deep enough to yield a palpable fremitus, auscultation of the sounds may give information not otherwise obtainable. It is well to learn how to correlate and do these two examinations synchronously.

ACCESSORY OR ADVENTITIOUS RESPIRATORY SOUNDS In addition to the natural breath and voice sounds and the changes these undergo in disease, certain sounds occur, inside and outside the lung, wholly additional to these. Of such adventitious respiratory sounds, two great groups are distinguished: (1) rales or crackles and rhonchi, and (2) friction sounds All rales are caused by moisture in the lungs but they are classified as (1) rhonchi and (2) rales.

Rhonchi and Rales. These sounds arise during respiration from interference with movements through the air passages of the air breathed. These interferences with the movements of the breathed air result from the presence of fluid, mucus, serum, blood, or water in bronchi and in cavities, leading often to the formation of air bubbles which may interfere with the movement of different masses of mucus or secretion and thus add noise The sudden separation of sticky mucous membranes or the passage of air through abnormal local narrowings produces sounds.

These sounds may be loud or feeble, numerous or few, they are often inspiratory in time, though they may be audible during expiration On testing for the presence of rales, the patient is asked to take a deep breath and end it with a short cough. It is important to notice whether the rales disappear or are modified on coughing.

Rhonchi are long, whistling or snoring sounds that die away slowly They are due to the vibrations of tough mucus attached to the walls of the bronchi, or to the passage of the air through lumina narrowed by spasm of the bronchioles or by swelling of their mucous membrane. They are often accompanied by palpable vibration of the thoracic wall The sounds, when low pitched, have a snoring character and are termed sonorous rhonchi If these sounds are high pitched, they are more whistling or piping in character and are termed sibilant rhonchi

Rales arise when fluid is present in the air passages They are crackling or bubbling sounds. In contrast with the more continuous, chiefly expiratory, sibilant and sonorous rhonchi, rales are interrupted, bubbling or crackling sounds, heard during inspiration.

The *moist rales* are sometimes classified according to the apparent size of the ... those next in ... ound of the ... of the hair between the fingers close to the ear.

The *crepitant rale,* no matter in which condition it is met with, is believed to be due to the opening up of collapsed air sacs or minute bronchioles. It is distinguishable from other moist rales chiefly by the short duration, or small size, of each of the successive crepitations, and by the large number of crepitations attending each inspiration.

Ringing or consonating rales are bubbling sounds arising in a cavity or in a larger bronchus and well propagated to the surface through infiltrated pulmonary tissue; the higher tones are strengthened through resonance in the bronchi. This ringing character of a rale is therefore of diagnostic importance in infiltrations of the lung Consonating rales occur under the same conditions in general as does bronchial breathing.

Metallic ringing rales occur under conditions similar to those in which a metallic clang on percussion and metallic bronchial breathing occur The so-called *metallic tinkling* is a single sound heard intermittently by the physician or the patient. It occurs most often in pyopneumothorax or in large tuberculous cavities.

PLEURAL FRICTION SOUNDS. Pleural friction sounds arise during respiration from the rubbing together of the pleural surfaces, roughened by some pathologic process such as fibrinous or inflammatory exudates.

These sounds are heard most frequently when the pathologic process is situated between the costal pleura and the pulmonary pleura; between the pulmonary pleura and the mediastinal pleura; or between the pulmonary and the diaphragmatic pleura The sounds may be fine, coarse or scratching or creaking They may be intense or feeble.

The softer, gentler friction sounds may sound like vesicular breathing; the coarser, crackling friction sounds may sound like rales. The pleural friction sounds, however, are usually accompanied by pain, they sound as if they were close to the ear, and they are intensified by pressure of the stethoscope They are often accompanied by a palpable friction fremitus. They do not disappear, nor are they modified on coughing Pleural friction sounds indicate the presence of a dry pleurisy in the region in which they are audible Friction sounds sometimes become audible in tumors of the pleura, or when the pleura is abnormally dry, as in severe dehydration.

Near the heart pleural friction may be heard which is synchronous with the heart's action, owing to the rubbing of the pericardial pleura against the adjacent pulmonary pleura. This is termed pleuropericardial friction

SUCCUSSION SPLASH COIN SOUND When the pleural cavity contains both liquid and air, and the patient is given a vigorous shaking while the physician listens to the thorax, a splashing sound is heard. This is termed the succussion splash The patient may be able to hear it and to produce it at will and may complain of it Even if this splash has never been heard by the physician, he should know about it in order to interpret it if the patient complains of it This splash is different from the one similarly produced in the stomach

A succussion splash is usually due to pneumothorax, it is occasionally heard in the absence of pneumothorax, when large cavities exist in the lung

The coin sound is hardly a diagnostic test It is elicited by percussing with coins on the back of the thorax at the level of a cavity and by listening with a stethoscope in the front of the thorax at the same level

Roentgenographic Examination of the Thorax. The *efficiency and limitations* of roentgenographic examination of the chest in the diagnosis of thoracic diseases by this means have been summarized by Rigler essentially as follows.

1 Pulmonary edema can be detected before the onset of appreciable symptoms or within a few hours thereafter It is detectable in the roentgenogram from 6 to 12 hours before the appearance of physical signs

2 Pleural effusion in amounts of 100 ml or more can be detected if proper technic is used This amount is compared with 500 ml of fluid necessary for demonstration by physical examination

3 Bacterial pneumonias give roentgenographic evidences of their presence in as short a time as 2 hours, most frequently within 6 hours, and almost invariably within 12 hours of the onset of definite symptoms.

4. Atypical or virus pneumonias may give no distinctive roentgenographic findings for 24 to 48 hours after the onset of symptoms.

5 Pulmonary tuberculosis of the ordinary chronic type is not demonstrable until 8 to 20 weeks after the exposure

6 Acute miliary tuberculosis invariably produces symptoms before the development of roentgenographic signs The latter may not be present for as long as 7 weeks after the onset of symptoms

7. Nodular lesions such as those produced by metastasis or nodular tuberculosis are demonstrable when their diameter is 3 mm or larger Even lesions of this size will

not be seen if multiple films in various positions are not made or if the lesions are unfavorably located

8 Metastatic lesions of miliary size, such as those produced by miliary tuberculosis, may not be visible until numerous or large in size.

9. All metastatic lesions are roentgenographically visible before the onset of symptoms or physical signs

10. Bronchogenic carcinoma almost invariably gives positive roentgenographic signs when symptoms are present, if thorough examination is done. There are a few exceptions to this rule In most instances roentgenographic evidences of abnormality will be present before the onset of any respiratory symptoms due to bronchogenic carcinoma Complete examination is necessary, however, to establish these evidences.

Reliability of interpretation of roentgenographic evidence of diseases of the lungs and pleurae requires training, skill and experience. The clinical management and even the details of treatment in thoracic disease often are based on the interpretation of shadows observed in roentgenograms. Physicians may hesitate to question the reliability of this method of examination, although they realize well the fallibility of other diagnostic procedures that appear less mysterious to them. Shadows that appear on films must be interpreted in pathologic terms.

An editorial in the *Journal of the American Medical Association* of December 29, 1951, discussed a project designed to record different opinions in regard to interpretation of roentgenograms of the chest. The project involved the recording of opinions by six experienced observers, three of whom were radiologists and three of whom were internists, regarding the stability of lesions of pulmonary tuberculosis as recorded on single roentgenograms (postero-anterior projections) taken at intervals of three months Each observer independently reported his opinion of each pair of films and subsequently re-examined the same series of films without reference to his original interpretation. The data thus recorded were analyzed by competent biostatisticians who were able to measure the inconsistencies of interpretation and relate the scores of each reader with the others and with his own previous opinions It was revealed that a second observer will disagree with the first observer in about one third of all instances and, what is more surprising, when the same observer reviews the same film a second time after an appropriately long interval, he will find disagreement between his two opinions in about one fifth of cases studied

These results in no way decrease the recognized necessity and value of roentgenographic examination of the chest, but they do emphasize the fact, long known to many physicians experienced in thoracic disease, that clinical management of thoracic disease must be based on many types of clinical and laboratory data and not on roentgenography alone Furthermore, the single postero-anterior chest film frequently does not constitute complete roentgenologic examination, for fluoroscopy, stereoscopy, tomography, and specially projected views may add materially to the accuracy of the examination in special circumstances However, with all of this information available, it must be realized that there is no substitute for the clinician, whose difficult task involves synthesis of different types of evidence in formulating a program of management for the patient In dealing with thoracic disease, the physician relies heavily on roentgenography, but realizes that the opinion of the dynamic status of pulmonary disease would in some instances be reversed if a second expert viewed the films or even if the same observer should submit a second opinion after he has forgotten the first report.

COMMENT

On examining the thorax by the physical methods heretofore described, it is appropriate to try to draw inferences regarding the air content of the underlying lungs and the physical state of the pleural cavities. Subsequently it is wise to seek the pathogenetic explanation of these physical conditions of the lungs and pleurae The methods of physical examination by employment of the special senses of the

physician are now known to be only approximately accurate but physicians, when trained, are grateful for the information they may give.

DISEASES OF THE PLEURA

Pleural Pain. The *parietal pleura* is innervated by sensory nerve fibers from the intercostal nerves. The ability to locate sensory impressions by the pleura is acute everywhere but seems more highly developed in the anterior and lateral aspects

The *peripheral regions of the diaphragmatic pleura* derive their sensory nerves from the phrenic nerve and the last six intercostals. The intercostals supply a peripheral rim of the diaphragmatic pleura, which is 1 to 3 inches (2.5 to 7.6 cm.) wide anteriorly, and a segment corresponding to the posterior third of the membrane. Irritation of the areas gives rise to pain in the lower part of the thorax on the same side and in the lumbar region or in the abdomen. The *central portion* is innervated by the phrenic nerve. Irritation of this portion sets up pain in the neck

The afferent impulses reach the cervical cord through the phrenic nerve trunk, and pass thence to the brain where the sensorium registers pain in the somatic segment corresponding to the entrance of the phrenic nerve; thus the pain is a referred pain

Disease or stimulation of the *peripheral or posterior portion of the diaphragm* produces pain which spreads over the lower part of the thorax and epigastrium, at times extending down over all of the abdomen on the same side

Capps has observed that the distribution of the pain depends on the degree of irritation and its prolongation. The more intense the irritation, the greater is the tendency of the pain to spread down over the lower portion of the abdomen, and in an occasional instance it may extend over both sides of the abdomen or to the lumbar region The pain may be associated with detectable hyperalgesia of the skin and superficial tissues on pressure

In some individuals who have diaphragmatic pleurisy the pain is referred to the neck along the area of the trapezius ridge The neck pain is spontaneous or produced by deep breathing or cough and is well localized by the patient with the tip of the finger Pressure over this point is painful

PARIETAL PLEURISY. The pain in pleurisy confined to the *upper lobes of the lungs* is always situated in the upper scapular and shoulder region In *pleurisy over the lower lobes* the pain is commonly restricted to the lateral and anterior aspect of the lower part of the thorax.

Localized pleurisy usually produces a sharp, stitch-like pain on cough or deep inspiration, directly over the region of the pleura involved, provided there is mobility between the parietal and visceral pleurae. Pleurisy without pain, even though a friction rub is present, may occur.

VISCERAL PLEURA The visceral pleura is insensitive

Pleurisy, for the sake of description, has often been referred to as dry pleurisy and wet pleurisy or pleurisy with effusion The nature of the effusion is designated by appropriate combinations of word roots For instance, the term serofibrinous pleurisy implies that the effusion is serous, empyema implies the presence of pus in the pleural cavity; pneumothorax, the presence of air, and hemothorax, the presence of blood

The wet and the dry types of pleurisy do not have etiologic implications, for in reality they may be but phases of the same disease These terms wet and dry are employed to designate the condition of the pleura at a particular time. As pleurisy runs its course, at one time or another it may pass through both the wet and the dry phases Fibrinous or dry pleurisy is the beginning phase of most pleurisies. It is the phase before an effusion into the pleural cavity takes place. After effusion dry pleurisy ceases to exist and there is present pleurisy with effusion If the effusion contains bacteria and is thus infected, the condition is empyema.

Dry Pleurisy. During the course of many diseases, pleurisy without a significant amount of fluid (less than 500 ml.) in the pleural cavity may occur. This is the so-called dry pleurisy. Dry pleurisy often is associated with the beginnings of pneumonia, less frequently with pulmonary abscess, gangrene, carcinoma, or infarctions, or with septicopyemia, rheumatic fever, or chronic nephritis, or it originates by extension from pericarditis, peritonitis, or hepatitis. It has some relation to tuberculosis, occurring sometimes as a primary infection, more commonly as a secondary event to a pulmonary tuberculous focus Carcinomatous metastasis to the pleura is soon followed by pleural effusion.

The first complaint by the patient who has a pleurisy is stitch pains in the side, usually in the neighborhood of the nipple, increased by movement and especially by inspiration, and accompanied by a dry and painful cough. Both cough and respiration are restrained, and the patient bends toward the affected side in order to minimize the pain For the same reason the breathing is hurried, shallow, jerking, and mainly abdominal in type. Fever is usually present, but the temperature seldom exceeds 101 F (38 3 C) and in mild illness may hardly rise above the normal There may be a moderate leukocytosis

On examination of a patient who has pleurisy there may or may not be a palpable friction fremitus. On auscultation a friction rub of variable intensity can be heard. The sound is audible during both expiration and inspiration. The pain and sounds are both increased on pressure over the affected part by the stethoscope or examining hand Hiccough is common Care should be exercised in order to differentiate the sounds of a dry pleurisy from those caused by the skin slipping under the stethoscope, a muscle sound, an atelectatic crackle, and hair on the chest. A dry pleurisy may disappear in a few days or it may last for weeks or even for months

The diagnosis is established from the foregoing findings and from roentgenologic examination.

Wet Pleurisy (Pleurisy With Effusion) Pleurisy with effusion usually follows acute pleurisy There is inflammation of the pleura, associated with a fluid exudate The fluid may be serous, serofibrinous, serohemorrhagic, purulent or putrid

Symptoms. The general symptoms of pleurisy may not be pronounced. The fever is rarely high, it may be continuous or remittent, and the temperature usually falls by lysis In some younger patients, and often in the aged, the onset of pleurisy is insidious There may be no complaint at all, or the patient may complain of nothing more than a little shortness of breath, and on physical examination the true nature of the illness is discovered The most constant general symptom of pleurisy is pain It is sometimes severe at the beginning and is increased by any movement, especially by deep inspiration, coughing or sneezing As soon as enough effusion develops to separate the surfaces of the pleura, the pain ceases. The pain may be referred to the back or the thorax, to the shoulders and arms, and occasionally into the abdomen The pain may erroneously be thought due to intercostal neuralgia, muscular rheumatism, or an acute surgical condition within the abdomen Chills or chilly sensations are common and sweats occur, especially during remissions of the fever and at night Digestive disturbances, including anorexia and nausea and vomit- [illegible] than in those who [illegible] ease in the amount [illegible] rine is the result of [illegible] mouth When the pleural exudate is being absorbed, it rarely can be absorbed fast enough to increase the output of the urine

Examination. When the patient is examined, it is noticed that the posture may be characteristic The patient has less pain, usually, if he lies on the affected side and assumes a diagonal position so as to give more freedom for expansion of the

lung on the healthy side If there is an extensive effusion, there may be orthopnea, and the sitting position is therefore assumed. When the effusion has developed fully, the scapula on the diseased side stands a little high and there is a slight lateral curvature of the spinal column, with concavity toward the healthy side The skin over the affected region may be stretched. On inspiration there is a lagging on the diseased side and the expansion is less The intercostal spaces may be widened, and Litten's phenomenon is absent. The veins of the neck are distended, and the apex beat of the heart is visible and can be seen displaced toward the side opposite the effusion On palpation, there are often changes in vocal fremitus However, an interpretation of vocal fremitus in pleurisy with effusion is difficult. If the effusion reaches any considerable size, on percussion there is dullness or flatness over the effusion. The upper limit of flatness and increased resistance on percussion assumes a typical curve, the upper part of the curve reaching its highest level at the posterior axillary line, whence it curves downward and forward toward the middle line in front. This line sometimes takes the form of a letter S turned on its side The effusion may fill a large part of one pleural cavity, then there is dullness over the whole side of the thorax, from base almost to apex One of the most important signs to be found in examining a patient who has pleurisy with effusion is the increasing intensity of the dullness or flatness or a feeling of resistance on percussing from above downward with the finger tips

On auscultation of the thorax, occasionally there are distant breath sounds or bronchial breathing, bronchophony and often rales may be heard. Accentuation of the breath sounds on the normal side is theoretically present, but practically this distinction usually cannot be made. Egophony is rarely heard

Diagnosis. The diagnosis of pleurisy with effusion is confirmed and often made by a roentgenographic examination Small effusions (less than 500 ml.) which cannot be determined on physical examination always are revealed in roentgenograms of the thorax If roentgen rays are not available, it is advisable to make an exploratory puncture when pleurisy with effusion is suspected to exist. There are several atypical forms of pleurisy with effusion which may exist as circumscribed pockets along the diaphragm or the interlobar portions of the lung, or the disease may be largely confined to the pleura along the mediastinum In any of these atypical forms of pleurisy with effusion, when there are no symptoms of pleurisy, exploratory puncture should always be considered, whether or not the pleurisy is a part of a so-called polyserositis In obscure infections the possibility of a small empyema, which cannot be differentiated from pleurisy with an effusion in any other way except by the exploratory needle, makes this diagnostic procedure imperative.

Bacterial Infections of the Pleura. Empyema. There are many bacteria which are capable of producing empyema Pleural infection is very commonly associated with lobar pneumonia and other pneumococcal infections These organisms gain access to the pleural cavity by extension from the lungs. Likewise tuberculous empyemas occur in pure form or as mixed infections

Empyema may occur during the course of septicemia. The *Escherichia coli* and *Salmonella typhosa* and paratyphi groups of organisms may invade the pleural cavity, particularly if there is peritonitis from these organisms *Pasteurella tularensis* and *Brucella* have been found in empyemic fluid

In still other instances streptococcal, staphylococcal, and pneumococcal empyemas and septicemia may follow a pneumonia or a pulmonary abscess caused by these organisms

The hemolytic streptococcus may reach the pleural space by direct extension from streptococcal pneumonia In some instances, however, the so-called primary empyema is associated with streptococcal bacteremia

Symptoms. Pleurisy is often an early manifestation of pneumonia and is evidenced as a stitch and later a pain in the lower part of the thorax The pain is usually

lost during the course of the pneumonia, not to recur until after the crisis or lysis and then only if there is a pleural infection as a complication of the pneumonia.

Empyema may make its appearance during the course of pneumonia. Often the febrile course of the pneumonia is unduly prolonged. The patient continues to show evidence of toxemia as manifested by weakness and marked leukocytosis, all of which are not evident until the course of the illness is obviously too prolonged for pneumonia.

In the usual instance, however, the empyema occurs after the pneumonia has run its course The patient's temperature and leukocyte count have reached normal limits. After one to two weeks of seemingly satisfactory convalescence, fever again appears, accompanied by profuse sweating. There may or may not be pleural pain The leukocyte count increases and a mild secondary anemia is present.

In those who have both pneumonia and bacteria which precede the pleural infection the diagnosis of *pyemia may have already been made* These patients are critically ill and the mere presence of empyema is of no importance so far as the outcome is concerned.

When a large quantity of foul smelling pus is expectorated there is an extension *of an empyema to form a bronchial fistula* (putrid empyema).

EXAMINATION. On examination of the thorax by physical means there may be a sufficient amount (500 ml.) of pleural effusion present to produce characteristic physical findings More frequently, however, there is too small an amount of pus present to be definitely detected by physical examination.

In other instances the signs of pleural effusion are masked by an underlying pulmonary consolidation

In instances in which surgical treatment is contemplated, the introduction of 10 ml of heavy iodized oil such as Lipiodol is a useful maneuver for determining the size and the most dependent portion of the empyematic cavity The heavy oil sinks to the most dependent portion of the empyema pocket. Postero-anterior and lateral films made with heavy exposure and with the patient in the upright position will indicate the optimal point at which to secure dependent drainage of the cavity

If there have been evidences of rupture of an empyemic cavity into bronchus such as the expectoration of quantities of pus a bronchopleural fistula may be present. The bronchopleural fistula may be demonstrated by the injection of 2 ml of a 1 per cent aqueous solution of gentian violet at the time of the diagnostic thoracentesis. If a fistula exists, the dye will appear in the sputum within 24 to 48 hours after injection

DIAGNOSIS The diagnosis is usually made on the basis of roentgenologic examination. A pleural exudate following pneumonia requires thoracentesis to distinguish between empyema and the sterile effusion which occurs after lobar pneumonias. The aspirated fluid is cultured bacteriologically to demonstrate with certainty the nature of the causative organism The effusion in instances of lobar pneumonia is usually sterile. When the effusion is sterile, no treatment is necessary.

Encapsulated empyema occurs along the pleural surfaces, usually between the lobes of the lungs. The presence of an encapsulated empyema can be established *only by roentgenologic examination and aspiration of the encapsulated pus*

COMPLICATIONS OF EMPYEMA. Infection of the thoracic wall is more likely to develop in those who have large abscess of the lung with profuse external discharge in the putrid type of empyema.

Empyema *necessitatis is the spontaneous rupture of an empyema* through the parietal pleura into the thoracic wall. Eventually the pus breaks through the skin. This condition is rarely encountered except with tuberculous and actinomycotic infections.

A bronchopleural fistula *may make its way to the surface of the thoracic wall,*

or it may drain into the bronchial system. Occasionally an empyema may drain completely by this route and heal spontaneously.

Septicemias and pyemias may either precede or follow empyema.

Tuberculosis of the Pleura. The tuberculous pleurisies occur in (1) those who have recognizable pulmonary tuberculosis and (2) those in whom pulmonary tuberculosis is not recognized There may or may not be a pleural effusion.

Two factors according to Meyers seem to be necessary for the development of a tuberculous pleural effusion: (1) An individual must be sensitive to tuberculin by having or having had tuberculosis. (2) The tuberculin must reach the pleural space. The tuberculin probably reaches the pleural space by the rupture of a small caseous pleural tubercle.

When a subpleural tuberculous focus enlarges and involves the pleural membrane, pleuritis ensues A firm scar binds the visceral and parietal pleurae, forming a pleural adhesion. Occasionally with the onset of pleural inflammation there is a rapid accumulation of serofibrinous exudate in the pleural space, and if the quantity of this exudate is sufficient (500 ml or more), a detectable clinical pleural effusion is present

SYMPTOMS. The general symptoms of pleurisy have been described in discussions of the various forms of pleurisy Dry pleurisy is manifested by pain on respiration The pain is well localized, and is aggravated by deep breathing, coughing, and movements of the thorax The pain from involvement of the diaphragmatic pleural surface is often referred to the posterior midshoulder region of the affected side. The pain often begins abruptly and increases rapidly in intensity.

There may or may not be fever When present, fever is irregular in its appearance and is rarely high. It increases as effusion takes place, and in extremely acute tuberculous pleurisy the temperature may reach 105 F (40.5 C). If a large effusion accumulates, symptoms of increasing intrathoracic pressure appear.

EXAMINATION. Physical examination may reveal reduction of respiratory excursion in the involved half of the thorax. A pleural friction rub or fine dry pleural crackles are frequently heard

On development of pleural effusion the friction rub disappears, to be replaced by the signs of fluid, dullness to flatness on percussion, reduction or absence of breath sounds, voice sounds, and tactile fremitus, and egophony The trachea and other mediastinal structures may be shifted away from the side of the effusion, the degree of displacement depending on the amount of fluid present and the mobility of the mediastinum

In tuberculous pleurisy, except during the very acute manifestations of the disease, the total number of leukocytes is usually within the normal range. During the very acute phase of the disease there is a polymorphonuclear leukocytosis which quickly subsides

A tuberculous effusion when withdrawn is a straw-colored fluid. Leukocytes in the fluid ordinarily number 500 to 3,000 per cubic millimeter, nine tenths of which are lymphocytes The fluid may contain blood.

Guinea pig inoculation or culture on special media for tubercle bacilli should be a routine procedure, but by all methods of examination the results in 30 to 50 per cent of these fluids are negative for tubercle bacilli.

DIAGNOSIS Roentgenologic examination demonstrates evidence of the pleurisy. Tuberculous pleuritis may occur in a patient who has evidence of an active lesion in the lung. In this instance the diagnosis of tuberculous pleurisy is obvious

Dry tuberculous pleurisy, however, may and often does exist in the absence of demonstrable pulmonary tuberculosis and without pleural effusion

A negative tuberculin reaction which remains negative for a few months after the attack is good evidence against a tuberculous etiology.

If a large effusion is present when the patient is first seen, a roentgenologic

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A bronchopleural fistula may make its way to the surface of the thoracic wall,

the subsequent tuberculous empyema may be limited, but a mixed infection may develop later. Most of the patients in whom spontaneous pneumothorax develops in the course of tuberculosis become seriously ill. All of them have fever, and without exception a pleural exudate appears soon after the onset About half the patients die within one month, and probably fewer than 1 in every 10 regain health

EXAMINATION. On examination of a patient who has a pneumothorax, the affected side may be distended and nearly or absolutely immobile on respiration. The apex beat of the heart is displaced toward the normal side unless the mediastinum is immobile The vocal fremitus is enfeebled or absent. The trachea may be displaced toward the normal side. The percussion note is hyperresonant but it varies according to the tension of the gas in the pleural cavity. The affected side may be considered to be normal on percussion while the normal lung is thought to be the one affected On listening at the back of the thorax while someone else taps one coin on another in front, a distinct, metallic, echoing sound is heard. If there is a considerable amount of fluid or pus present in the thorax, the percussion dullness may be bounded by a horizontal line, and this line remains horizontal, irrespective of change in posture of the thorax. On shaking the patient, a metallic splashing sound may be audible. When a pulmonary fistula is patent, and is below the surface of the fluid in the pleural cavity, on the patient's lying down, or standing, the sound of gurgling fluid may be heard On auscultation over a pneumothorax the breath sounds may vary from markedly feeble to loud and amphoric.

DIAGNOSIS. If no abnormalities are found on physical examination, the roentgenologic examination will reveal the presence of pneumothorax. Fluid accumulates rapidly in the pneumothorax pocket It is important to determine whether the bronchopleural communication remains open, for if there is a widely open bronchopleural communication, withdrawal of large volumes of air does not alter the intrapleural pressure

The early management of these patients is concerned with removal of the pneumothorax air as needed In the mildest forms of the disease treatment may not be necessary.

Rheumatic Pleurisy. Rheumatic fever causes a small number of cases of serofibrinous pleurisy with effusion

Rheumatic fever attacks serous membranes selectively; for instance, the synovial membranes, the endocardium and the pericardium are common sites of rheumatic infection In a few cases the pleural membrane also is affected, with the production of a fibrinous pleurisy often quickly followed by serous pleural effusion. This sequence of events is particularly likely to occur in the presence of rheumatic *pneumonitis or pericarditis, whence the infection apparently spreads directly* or by extension along the lymphatics

Those who have rheumatic pleurisy have had rheumatic fever, and in all but a very few the pleural involvement occurs in the course of an acute exacerbation of symptoms The pleuritis may be preceded in onset by polyarthritis. However, in some patients the joints become involved after the onset of the pleurisy. The symptoms in this latter group of patients are those of rheumatic polyarthritis accompanied by the development of pleuritic pain Characteristically the patient is very ill, with high fever and dyspnea Rheumatic pleurisy often co-exists with pericarditis. Rarely a subacute or chronic rheumatic pleuritis is observed.

EXAMINATION. Early in the course of rheumatic pleurisy a pleural friction rub may be heard, but this is quickly superseded by signs of effusion In almost all of these patients examination by physical means reveals evidence of rheumatic mitral heart disease

A history of previous rheumatic fever or the presence of a rheumatic cardiac lesion is the chief clue in making a correct diagnosis. Rheumatic pleurisy is identified when a serous pleural effusion develops in the course of rheumatic fever. The

examination is made after thoracentesis. A definite diagnosis of tuberculous pleurisy is made by demonstration of the tubercle bacillus by inoculation of a guinea pig.

Histologic studies of the cells in the sediment should be made for presence of malignant cells

Tuberculous Empyema. Tuberculous empyema exists if the pleural exudate is definitely purulent and contains tubercle bacilli in sufficient numbers to be demonstrable in an unconcentrated smear. A tuberculous empyema is termed *simple* when the tubercle bacillus is the sole infecting organism, and *mixed* when in addition one or more other types of pathogenic bacteria are present in the pleural cavity.

1. ***Simple Tuberculous Empyema.*** The visceral and parietal pleura are considerably thickened by fibrous tissue together with caseous material. The pleural pus contains only tubercle bacilli, which are found by direct smear examination

Tuberculous pleural empyema may occur spontaneously, but often is present in those who have received artificial pneumothorax for pulmonary tuberculosis

The pathologic process is a subpleural tuberculous focus which has spread by caseation, liquefaction and rupture into the pleural cavity

At the onset of the empyema there is some fever, and often pain in the chest. The acute empyema may come on abruptly, usually soon after the induction of pneumothorax, owing to extensive pleural caseation In these instances the temperature rises rapidly to 104 F (40 C) and chills occur. Pleural pain in the involved side is an early symptom. The fever may persist for several weeks and subside gradually. Between these mild and severe attacks of the disease, gradations in severity of the clinical manifestations may exist.

The mortality rate in all cases of simple tuberculous empyema has been high, from 30 to 40 per cent

The diagnosis of simple tuberculous empyema is made when the presence of fluid in the pleural cavity is determined and aspiration yields a turbid or purulent exudate containing acid-fast bacilli on direct culture or smear, but giving sterile cultures for other bacteria.

2. ***Mixed Tuberculous Empyema.*** In the mixed tuberculous empyema the exudate is purulent and may contain a wide mixture of organisms

The pleural infection arises from a rupture of a caseous focus in the visceral pleura of a tuberculous lung, with the production of a bronchopleural fistula When such an event occurs, tubercle bacilli as well as the pyogenic flora of the bronchial tree reach the pleural cavity in large numbers

The symptoms of the mixed tuberculous empyema are the same as those of simple tuberculous empyema but more severe

The presence of a mixed infection may not be suspected until cultures of the pus reveal the pyogenic organisms The diagnosis of tuberculosis is suspected and proper isolation and care of the patient have been executed long before the presence of tubercle bacilli has been demonstrated by cultures

The prognosis is grave, more than 70 per cent mortality is to be expected

Tuberculous Spontaneous Pneumothorax. A region of tuberculous caseation originates in the subpleural tissues and extends to the pleural membrane, liquefies it and ruptures into the pleural space When rupture takes place, air, tubercle bacilli, and other microorganisms from the bronchial passages are admitted to the pleural cavity

SYMPTOMS. The patient, who is known to be suffering from pulmonary tuberculosis, has a sudden pain in the chest, becomes dyspneic and cyanotic and experiences varying degrees of shock In those who survive the initial episode, chills and fever ensue

In a few cases the pleural opening is small and closes rapidly. When this occurs,

which leave a moderate pleural fibrosis which persists. At times pleural effusions alone occur which are absorbed, leaving no evidence of their presence.

The findings on examination depend on the presence or absence of pneumonitis and pleural effusions.

Diagnosis depends on the status of the lung and pleura before roentgen therapy. If the examinations of the lung and pleura were recorded before roentgen therapy, and during the therapy if no other reason for the pleural changes occurred, it may be assumed that the pleurisy resulted from the irradiation therapy.

Traumatic Pneumothorax. Direct violence may cause pneumothorax by. (1) puncture of the lung by the sharp end of a fractured rib; (2) blows and crushing injuries without puncture of the thorax· in these injuries there are rupture of the visceral pleura, and intrapulmonary alveolar tears. The air then makes its way along the bronchovascular bundles to the hilus and reaches the mediastinum, causing mediastinal emphysema Secondary rupture of the mediastinal parietal pleura then produces pneumothorax; (3) penetrating wounds, and (4) artificial overinflation of the lung The use of excessive positive pressure in intratracheal anesthesia and pulmotors can produce pneumothorax.

In most of the instances caused by trauma the amount of air entering the pleural space is moderate or small. However, massive tension pneumothorax is occasionally seen.

SYMPTOMS. Often there is shock and this masks all other symptoms If there is no shock, pain in the injured side of the thorax is severe Dyspnea and cyanosis are severe if the pneumothorax is large In those who have small partial collapse, no symptoms in addition to those of the injury are observed

EXAMINATION Physical examination, in pneumothorax of moderate or large size, reveals hyperresonance to percussion which is often not great. The breath sounds are reduced or absent over the involved side of the thorax When a pneumothorax is extensive, the heart and trachea are frequently found to be displaced away from the side of the collapse. Signs of fluid in the pleural cavity are due to intrapleural blood from the site of injury Subcutaneous emphysema is a common occurrence in traumatic pneumothorax It usually develops when a break in continuity of the parietal pleura allows the escape of air from the pleural space which then makes its way to the subcutaneous tissue and may spread widely over the body. If extensive, subcutaneous emphysema is painful

DIAGNOSIS The presence of air in the pleural cavity is determined by the combined use of physical and roentgenologic methods The roentgenologic method is the only one by which the degree of collapse can be accurately determined

Chylothorax. Chylothorax consists of the accumulation of chyle in the pleural cavity This fluid has the appearance and stability of a solution of homogenized milk It contains varying amounts of fat (2 to 3 per cent) which are determined by the Babcock test as employed by dairymen

Injuries produced by hyperextension of the spinal column may rupture the thoracic duct After the injury a latent period of weeks may pass before fluid appears in the pleural cavity. The delay is due to retropleural accumulation of chyle. This chyloma appears as a mediastinal mass in the roentgenogram. The chyloma ruptures into the pleural space and chylothorax ensues. Chylothorax, like chyluria, may occur spontaneously.

Occasionally a mediastinal lymphosarcoma or Hodgkin's disease may completely obstruct and rupture the thoracic duct and produce chylothorax

The development of some instances of chylothorax is characteristic The onset of pleural pressure symptoms such as dyspnea, cyanosis, tachycardia, and a sense of tightness in the chest is severe Associated with these symptoms is a decline in weight, due to the loss of large amounts of digested and absorbed fat. In some instances the wasting and exhaustion of the patient continue to progress, and the

fluid removed by thoracentesis is an exudate which clots rapidly. It is sanguineous in appearance in more than half the cases. Leukocytes in the fluid number from 500 to 5,000 per cubic millimeter and a differential count usually shows a very slight preponderance of polymorphonuclear cells over lymphocytes. Cultures of the exudate are sterile. This condition must be differentiated from other pleurisies by the presence of other symptoms or signs of rheumatic disease.

PLEURISY DUE TO FILTRABLE VIRUSES

Epidemic Pleurodynia (Epidemic Myalgia). This disease is characterized by an acute febrile illness of brief duration whose chief symptom is severe thoracic pain indistinguishable from that of pleurisy. The disease has occurred in small sporadic epidemics, which usually are observed during the warm months of the year The incidence is chiefly among children and young adults.

From stored throat washings from those who had pleurodynia, Miller and associates of Harvard University and Tufts College recently isolated a virus antigenically related to the Connecticut 5 virus previously isolated by Melnick from a case of nonparalytic poliomyelitis

Epidemic pleurodynia has an abrupt onset with fever accompanied by a chill Pain on breathing or coughing appears simultaneously and is limited to the lower intercostal regions of one side. However, instances with bilateral pain, headache, abdominal pains and stiffness of the back and neck have been recorded

The temperature reaches 101 to 104 F (38.3 to 40 C) and the fever and pain persist, as a rule, for 12 to 48 hours Thereafter the symptoms subside rather rapidly, but after an interval of 2 days or so about one fifth of the patients have a second paroxysm of pain and fever identical in character with the first, but usually somewhat less severe. After this, recovery is prompt, there being no complications Death from epidemic pleurodynia has never been reported

Examination often reveals that the patient has a moderately red throat, but cough is not common. The involved side of the thorax may reveal muscle guarding and there is tenderness on pressure in the intercostal spaces over the painful region Pleural friction rubs on auscultation are inconstantly present.

DIAGNOSIS. The course of the disease and its occurrence as part of an epidemic must decide the diagnosis. It would be impossible to identify a sporadic case of epidemic pleurodynia Leukocyte counts reveal a mild leukopenia during the active stage of the disease

DISEASES OF THE PLEURA DUE TO TRAUMA OR PHYSICAL AGENT

Traumatic Serofibrinous Pleurisy. *Serofibrinous pleurisy* may develop as a sequel of direct trauma to the thorax In general it appears that the serofibrinous pleurisy most commonly is associated with a subpleural hematoma The common causes of serofibrinous pleurisy are fractures of ribs with the formation of hematoma subpleurally at the site of the fracture, with or without actual penetration of the parietal pleura by the fractured fragments of bone However, hematomas may occur from contusion of the thoracic wall without rib fracture. Likewise contusion of a lung, due to either direct or contrecoup violence, with hematoma beneath the visceral pleura, may be associated with serofibrinous pleurisy It seems that the size of the effusion is ordinarily small and the fluid is blood stained. Cultures of these effusions are sterile unless secondarily infected by pyogenic bacteria

Pleurisy Following Irradiation Therapy. After intensive roentgen therapy to the thorax a pulmonary reaction may occur. In the beginning there is the appearance of a pneumonitis which progresses slowly, resolves slowly, and heals poorly, for sometimes there is left an increase in fibrous tissue in the involved region of the lung In some cases of this roentgen pneumonitis, changes develop in the pleura

Pleural Transudates. ***Venous Passive Congestion.*** The usual cause of passive congestion in the veins draining the visceral and parietal pleura is congestive cardiac failure. Constrictive pericarditis has a somewhat similar effect In the occasional case of obstruction of the superior vena cava, congestion of the parietal pleura develops because of interference with return flow through the azygos system.

The symptoms are those of congestive heart failure. The findings on examination by physical means are those of heart failure and fluid in the pleural space, especially on the right side of the thorax.

The fluid obtained by thoracentesis is a thin straw-colored fluid, relatively clear, and having a specific gravity usually less than 1.014. If the effusion has been present for some time, reabsorption of water may cause concentration of the proteins, giving a higher specific gravity. In uncomplicated cases the fluid contains very few cells, usually less than 500 per cubic millimeter, and these are lymphocytes. The presence of polymorphonuclear leukocytes and erythrocytes suggests the existence of a complicating pulmonary infarct or a secondary infection of the transudate, an empyema. An empyema in a patient who has heart failure is suggestive of a dispersion of infected thrombi from a bacterial endocarditis.

PLEURISY OF ENDOCRINE ORIGIN
(*Meigs' Syndrome*)

In the presence of benign fibroma of the ovary there may be associated a sterile serous pleural effusion and serous ascites. Women between the ages of 30 and 65 years complain of dyspnea and unilateral thoracic pain. There is no fever. Examination reveals physical signs of pleural effusion the presence of which is confirmed by the roentgenogram The ovarian fibroma is variable in size but can ordinarily be detected on pelvic examination

Thoracentesis yields a thin straw-colored fluid, which contains but few leukocytes—usually fewer than 1,000 per cubic millimeter—the majority of which are lymphocytes Cultures and inoculation of guinea pigs with the fluid are negative. Results of examination for neoplastic cells are negative.

The diagnosis is confirmed by the finding of fibroma of the ovary in the absence of heart failure or embolism A patient who is found to have an ovarian tumor with pleural effusion, everything else being negative for positive evidence of malignant disease, should have the pelvis surgically explored if there be an enlargement of an ovary Patients afflicted with Meigs' syndrome have recovered completely after removal of the ovarian fibroma.

SPONTANEOUS PNEUMOTHORAX

The term spontaneous pneumothorax implies that air has spontaneously entered the pleural space and thus produced a collapse of the lung Spontaneous pneumothorax despite its cognomen in the series of pneumothoraces usually results from rupture of an emphysematous bulla, situated on the surface of the lung, into the pleural space

The normally existing negative intrapleural pressure is an expression of the physiologic internal elasticity of the lung which brings it to a smaller volume while at rest. The lung remains expanded because of its internal atmospheric pressure, which is a greater force than this normal force of contractility of the lung When a communication develops between the pleural space and the atmosphere through an opening in the

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pleural cavity to compensate for the shrinkage, and pneumothorax results In an otherwise normal thorax the difference in pressure between the two pleural cavities causes a displacement of the mediastinal structures away from the side of the pneumothorax

condition is fatal within a few weeks. In other cases, after the initial accumulation of pleural fluid, the mediastinal pressure becomes stabilized so that pressure symptoms are no longer severe The pressure appears to reduce the leakage of the fluid into the pleural sac.

Some patients carry a large chylothorax and enjoy fairly good health However, most of those who have chylothorax die within a period of a few months.

Physical and roentgenologic signs are those of pleural effusion. The presence of chylothorax is established by thoracentesis. Aspiration yields a fluid having the appearance of milk. The Babcock test for fat reveals a fat content of from 1 to 2 per cent or more, which establishes the diagnosis

Hemothorax. In hemothorax the pleural cavity contains blood, little if at all diluted with serous exudate Hemothorax originates from many causes, trauma and malignant disease are the common agents.

After an intrapleural hemorrhage has taken place, the blood gradually undergoes a change in color (conversion of hemoglobin to bilirubin). If the blood withdrawn by thoracentesis is centrifuged, a yellow or brownish tinge in the supernatant plasma indicates that bilirubin has already been formed and therefore the hemorrhage must have begun at least a day or two or longer prior to the aspiration.

Hemopneumothorax. Hemopneumothorax is the combined presence of blood and air in the pleural cavity This condition is most frequently the sequela of traumatic pneumothorax, and the blood comes from an intrapleural wound

Hemopneumothorax, however, occasionally occurs in idiopathic pneumothorax, and more rarely in the tuberculous and emphysematous types of spontaneous pneumothorax If the amount of blood in the thorax is small, it will not affect the course of the pneumothorax.

A low-grade fever may be produced by pleural irritation and disintegration of blood In the rare instances in which severe hemorrhage has occurred, shock may ensue.

Except in those known to have tuberculosis, hemopneumothorax is suspected when a sizable effusion appears in the pleural cavity of a person who has a pneumothorax Aspiration of some of the fluid confirms the diagnosis

The blood is removed from the pleural space to prevent future fibrosis and calcification.

PLEURAL EFFUSIONS SECONDARY TO DISORDERS OF CIRCULATION

These effusions are usually sterile like those from the pneumococcus and rheumatic pleurisies Pneumococcal empyema occurs in those who have had untreated lobar pneumonia.

Pleural Effusion Due to Pulmonary Infarction. The occurrence of a pulmonary infarct is followed by an intense inflammation-like reaction of the pleura when the infarct is situated near the periphery of the lung. A thin layer of fibrinous exudate rapidly appears on the visceral pleura overlying the infarct Then a serous exudate begins to accumulate in the pleural space, the fluid developing rapidly and commonly becoming sanguineous from leakage of erythrocytes from the intensely congested infarcted tissue

Immediately after the infarct there may be no signs of pleurisy on examination by physical means Twelve to 24 hours after the accident a pleural rub, and later the signs of pleural effusion, will be present in all subpleural infarctions

The diagnosis is established by roentgenoscopic examination In case the pleural exudate is examined, it will reveal a leukocyte count in the fluid of 1,000 cells per cubic millimeter or less The fluid is sterile on culture and contains no tumor cells, and tubercle bacilli cannot be recovered by guinea pig inoculation

PLEURAL THICKENING

During the routine examinations of the thorax there may not be signs of pleural thickening Roentgenologic examination may, however, reveal some thickening of the pleura. These pleural thickenings are of varying degrees and extent. A chronic inflammation of the pleura with formation of new fibrous tissue, and with adhesions between two layers, in rare instances may extend to the point of obliteration of the whole pleural cavity on one side, with retraction of the thorax. The side of the thorax which is affected is shorter than the other. There is scoliosis with concavity toward the shrunken side. The shoulder on the affected side is depressed and the intercostal spaces are narrowed. There are diminished expansion, dullness on percussion, and enfeeblement of the breath and voice sounds and of vocal fremitus Litten's phenomenon is absent. As the side becomes shrunken, the mediastinum and the heart are drawn toward it If there be much thickening, an exploratory needle may have to be jabbed through a thick layer of tough, fibrous tissue In some instances of this type of pleurisy the whole pleura becomes calcified Adhesions to the diaphragm are often exquisitely demonstrated on roentgenographic examination

Commonly, however, there will be observed circumscribed adhesions only, usually to the diaphragm or at the bases of the lungs The etiology of these pleural thickenings is not known Great thickenings of the pleura are most often due to tuberculous pleurisy

If signs and symptoms of this type of pleurisy are present, they usually are minimal. At times, however, the patients may be slightly cyanotic, and they often have some dyspnea on exertion

MALIGNANT TUMORS OF THE PLEURA

Primary Malignant Lesions. The pathologists have complained of the difficulty in the histologic classification of primary pleural malignant tumors. These tumors may be called carcinomas, sarcomas, endotheliomas and mesotheliomas The manifestations of these tumors are not distinctive nor can the neoplasms be definitely separated from secondary metastatic malignant lesions

The metastatic tumors which involve the pleura are mostly carcinomas and sarcomas

The first symptom of pleural tumors is heaviness or fullness in the thorax, often a dull, aching sensation. Soon pain is associated with respiration, and it is sharp and cutting in nature Dyspnea, shortness of breath, cough, expectoration and loss of weight and strength follow in rapid sequence.

Fever, palpitation and tachycardia are common The evidence of cardiac embarrassment through mediastinal compression which may ensue is the presence of edèma of the extremities and ascites Ptosis, enophthalmus and contracted pupil (Horner's syndrome) may result from pressure on autonomic nerves.

In some instances on examination there is a tumor of the thoracic wall Decreased expansion of the thorax, edema of the arms and legs, abdominal ascites, engorgement of vessels of the thoracic wall and edema may have developed as a result of mediastinal compression and encroachment on the heart or large blood vessels

On percussion of the thorax either dullness or flatness will be elicited over irregular regions Often the neoplasm is diffuse or, if there is fluid in the pleural cavity, dullness and flatness may be extensive A high diaphragm on the side of the lesion usually can be elicited by physical means and indicates direct diaphragmatic or phrenic nerve involvement Auscultatory findings consist of diminished or absent breath sounds Rarely will there be rales, and pleural friction rubs are unlikely.

Occasionally, as a lung collapses, the consequent contraction of the pleural membrane will close the bronchopleural opening and thus halt the process at this point. The normal pressure relationships are somewhat re-established and the intrapleural pressure remains slightly negative as compared to the atmosphere.

The term tension pneumothorax indicates the building up of an intrapleural pressure greater than atmospheric pressure This serious condition is permitted to develop by a bronchopleural communication, a one-way valve action which allows air to pass only from the lung to the pleural space (Meyers).

Pulmonary Emphysematous Spontaneous Pneumothorax. In pulmonary emphysema there are often subpleural bullae containing air and communicating with the bronchial tree The visceral pleura is the outer wall of the blebs. Rupture of one of these subpleural bullae produces spontaneous pneumothorax. In these instances collapse of the lung is only partial. In cases of tension pneumothorax the increased intrapleural pressure is great enough to collapse even an emphysematous lung.

The patient who has emphysema suffers from severe pleuritic pain in one side. Dyspnea and cyanosis are evident except in the mildest instances of pneumothorax and vary in degree with the extent of the collapse Fever is uncommon and pleural effusion usually does not occur.

Physical examination reveals the signs of pneumothorax on the side of the pain When subcutaneous emphysema appears, it is ordinarily secondary to mediastinal emphysema; hence the presence of air is first observed in the tissues of the neck, from which it may spread. The diagnosis is established by the finding, on physical and roentgenologic examination, of pneumothorax in a patient suffering from pulmonary emphysema.

Spontaneous pneumothorax due to emphysema often recurs. There being no pleural inflammation at the time of the collapse, adhesions frequently do not form and the same or a different emphysematous bleb may rupture again In some instances multiple recurrences have been observed In a patient who has extensive emphysema, severe spontaneous pneumothorax may be fatal.

Idiopathic Spontaneous Pneumothorax. The term idiopathic pneumothorax is aptly applied because in the rare fatal instances of the disease necropsy has not disclosed a bleb or the point of pleural rupture. If a pleural rupture is demonstrated, it is the so-called subpleural vesicle, a local congenital weakness of the pleural tissues.

Idiopathic pneumothorax occurs in young, healthy adults The onset is with a sudden violent pain in one side of the thorax There may be shock The respirations are shallow and rapid The patient may have a slight fever for 2 or 3 days but none thereafter, and in many cases the temperature remains normal throughout

Physical examination reveals signs of pneumothorax on the side of the pain and, in marked instances, some degree of mediastinal displacement away from the side of the lesion

In idiopathic benign spontaneous pneumothorax, pleural fluid usually does not appear. In some instances a small amount of serous exudate develops If a large pleural effusion is found, the most likely cause is hemothorax, as a result of bleeding from the lung at the time of pleural rupture

Subcutaneous emphysema occurs occasionally in idiopathic spontaneous pneumothorax The subcutaneous air appears first in the neck and subsequently spreads

A diagnosis of idiopathic spontaneous pneumothorax is justified when the condition develops in the absence of trauma in a young patient who has no known preexisting pulmonary disease. A roentgenologic examination reveals and confirms the presence of a pneumothorax. The extent of a pneumothorax can be determined only by roentgenologic investigation.

in bed The pain is situated in the region of the epigastrium or just above the ensiform cartilage. The symptoms may be suggestive of gallbladder disease, ulcer, or *angina pectoris*.

The findings on physical examination depend on how large the hernia may be. If the hernia is large, there is thoracic tympany, and borborygmi are heard in parts of the thorax usually occupied by the lungs. In small hernias there are no signs on examination

The hernia is revealed by roentgenoscopic examination after the patient has ingested a barium meal In large hernias the diagnosis may be suspected from physical examination or the history or may be found on a routine roentgenogram of the chest.

When diaphragmatic hernias are discovered accidentally and are not causing symptoms, no treatment is necessary.

False Hernia. The false diaphragmatic hernias are always due to an arrest of development of the pleuroperitoneal membrane with a congenital absence of a part of the diaphragm Congenital defects of this kind occur much more frequently on the left side than on the right An absence of a part of the left half of the diaphragm permits the abdominal organs, such as the stomach and parts of the intestine and occasionally the spleen, the pancreas and the left kidney, as well as a portion of the liver, to enter the perforated pleural cavity In the extremes, most of the pleural cavity is occupied by these organs Such hernias vary in extent from this extreme to those with defects in the diaphragm which admit only small parts of the abdominal contents.

The symptoms are variable in degree and often none are present.

In extreme instances of diaphragmatic hernia, tympany on percussion and peristaltic sounds on auscultation on examination of the thorax are diagnostic. In those hernias which admit only a small portion of an abdominal viscus into the pleural cavity, the diagnosis is established by roentgenoscopic inspection after the patient has ingested a barium meal.

INFECTIONS OF THE DIAPHRAGM

Acute Diaphragmatitis. Acute diaphragmatitis is usually associated with acute infections situated either in the thorax or in the abdomen such as pneumonia and peritonitis, or with general disease of the body as a whole In other instances of acute diaphragmatitis the etiology is usually not known

There is an acute inflammation, with swelling of the muscle fibers, which may be limited to the muscle or may extend to its serous coverings Fluid may accumulate, followed by adhesions and obliteration of the cardiophrenic and costophrenic angles These inflammatory processes may destroy muscle, which is replaced by fibrous tissues, and thus the diaphragm partially loses its ability to function and appears flat rather than dome-shaped on roentgenoscopic examination

The disease may extend, however, so as to involve the diaphragmatic pleura, resulting in pleural effusion and even empyema. It may then extend to the visceral pleura, to the diaphragmatic peritoneum, and to the liver, and thus produce symptoms indicating the extension of the disease

The symptoms commence with a chill and fever followed by pain over the costal margins and in the shoulder region of the involved side. Often there are pain and soreness across the upper part of the abdomen The pain is intensified on inspiration and change in posture The symptoms are often very much like those of a pneumonia which affects the base of the lung or both lungs

The symptoms disappear within a few days but often recur at irregular intervals. Unless the lung is affected, there are little or no cough and expectoration There are often a loss of body weight, anorexia and constipation

The patient on examination may or may not appear ill. Limitation of motion or a partial immobilization of the diaphragm and the lower part of the thoracic

For practical purposes roentgenologic examination often sufficiently limits the diagnostic possibilities. The diagnosis as to the type of tumor is established by microscopic study. Malignant cells may be *demonstrated in the bloody pleural* fluid obtained on aspiration.

DISEASES OF THE DIAPHRAGM

Position of Diaphragm. The peripheral projection of the diaphragm adheres closely to the lower borders of the lungs (see pp 536 and 537).

The *diaphragm is elevated* by peritoneal fluid or air, or gas in the digestive tract; tumors, or pregnancy, conditions within the thorax, such as atelectasis, extensive pulmonary fibrosis and adhesions; interruption of a phrenic nerve; congenital muscular defects and myasthenia gravis.

The diaphragm may occupy a *low position* in acute diaphragmatitis; phrenic nerve irritation, as may occur in encephalitis, tetanus, tetany and singultus with peritonitis; visceroptosis and asthenias, pleural fluid, pneumothorax, emphysema, asthma and intrathoracic tumors.

The diaphragmatic muscle may be involved by acute infections. The pleural surfaces of the diaphragm often participate in the infections or malignant lesions of the rest of the pleural surfaces of the thorax. The peritoneal surface likewise participates in the malignant disease and infections of the peritoneal cavity.

DISEASES OF THE DIAPHRAGM DUE TO PRENATAL INFLUENCES

Congenital Eventration of the Diaphragm. *This condition* is called also elevation, dilatation, high position, insufficiency, relaxation of the diaphragm, and Petit's disease

Eventration of the diaphragm is often due to a congenital fault, which is a failure of the diaphragmatic musculature to develop on one side, usually the left side. In place of the muscle there exists only a thin membrane The pleural and peritoneal components are intact, but in the absence of muscle *the involved part* of the diaphragm yields to pressure.

The condition is characterized by an abnormally high position of one half of the diaphragm The high position is permanent and the diaphragm is intact The abdominal viscera are placed high and occupy space which topographically belongs in the thoracic cavity

There may be dyspnea, substernal pain, discomfort or pain after meals, and occasionally nausea and vomiting. Usually, however, there are no symptoms

On examination an increase in the respiratory expansion of the thorax in the region of the costal margins may be observed while the patient stands. This increase in inspiratory expansion is made less obvious when the patient is in the recumbent posture. Tympany may be elicited over the lower part of the thorax which is normally occupied by lung Borborygmi may be heard over the lower part of the thorax in positions where these sounds are not normally audible.

The diagnosis is established by roentgenoscopic study after the patient has ingested a barium meal.

In most cases of eventration of the diaphragm no treatment is necessary

Congenital Diaphragmatic Hernia. Congenital diaphragmatic hernias are separated on an anatomic basis as true hernias and false hernias

True Hernia. In a true diaphragmatic hernia the abdominal contents extend through the diaphragm into the thorax within the sac formed by the serous coverings of the diaphragm These hernias occur most frequently at the esophageal foramen. However, they may occur in any part of the diaphragm. They often result from congenital imperfections in the diaphragmatic muscle

Often there are no symptoms. In most instances of diaphragmatic *hernia, however*, pain is present when the stomach is full and often while th- patient is lying

Secondary Diaphragmatitis. Pneumonia and peritonitis are common causes of secondary diaphragmatitis In basal lobar pneumonia marked diaphragmatic changes occur, and in fatal instances of the disease the postmortem examinations often reveal waxy degeneration of the muscle fibers. In cases of bronchial pneumonia the diaphragmatic changes are slight and recovery is often complete.

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The weight of pleural effusion damages the diaphragm by producing stretching deformity and loss of elasticity. When fluid is present in the pleural space, there is a tendency for adhesions to form in the costophrenic angles and between the pericardium and the diaphragm, fixing the diaphragm in an abnormal position which impairs its function In cases of extreme diaphragmatic adhesions the heart may be displaced

In any chronic infection of the lung when dyspnea is out of proportion to the amount of pulmonary involvement, an impairment of diaphragmatic function is suspected as being at least partially responsible. In tuberculosis and pneumoconiosis bilateral diaphragmatic adhesions may result in marked restriction of the diaphragmatic excursion and thus dyspnea is inevitable.

SUBDIAPHRAGMATIC ABSCESS

Subdiaphragmatic or subphrenic abscess is a collection of pus beneath the diaphragm It is usually subsequent to some suppurative process within the abdomen Other causes, however, have included infection carried from some distant focus by the blood or lymph and invasion of the subphrenic space by extension through the diaphragm of a suppurative process within the thorax.

*The subphrenic portion of the body extends from the diaphragm to the trans*verse colon This region is subdivided by the liver and the arrangements of its peritoneal folds or ligaments, to form three subphrenic spaces on the right side and one space on the left

Location of Abscess The right side is more frequently involved than the left because the most frequent diseases preceding subphrenic abscess are lesions of the appendix, gallbladder and duodenum. There are occasions, however, when these lesions are followed by subphrenic abscess on the left side.

The microorganisms found on culture from subdiaphragmatic abscesses are, in the order of frequency, streptococci, gram-negative bacilli, staphylococci, *Escherichia coli,* Proteus and various micrococci

Symptoms The symptoms of subphrenic abscess depend on the combination of many variable factors and are therefore largely dependent on the symptoms *of the original lesion or on the postoperative discomforts incident* to a recent operative procedure These discomforts may accentuate, diminish, or completely mask the symptoms produced by the subphrenic abscess. The particular subphrenic space involved by the abscess, the onset of the disease, the general condition of the patient, the presence or absence of complications, and the nature of those complications present will influence the symptoms. The symptoms may be summarized as general reactions, local reactions and pleural reactions

The general reaction often is that of overwhelming infection. The onset is *sudden with fever, chill and fever* and the patient is seriously ill When the infection becomes localized, there is pain situated in the region of the diaphragm and the findings may simulate a pleurisy.

The pleural and local manifestations revealed by physical examination are often meager indeed despite the presence of intense pain with high fever. However, in some there is evidence of pleural effusion or pneumonia.

wall may be observed. In the beginning there are no abnormal auscultatory findings. *There is no descent of the diaphragm on inspiration.* A pleural effusion may be present.

As the disease develops and the diaphragm becomes immobile, there may be congestion at the bases of the lungs. Spasm of the transversus abdominis muscle is observed on palpation. Spasm of the muscle may be due to extension of the inflammatory condition into the fibers of muscle. The polymorphonuclear leukocytes range from 9,000 to 20,000 per cubic millimeter of blood after the symptoms are well established

The diagnosis of diaphragmatitis is suggested by the history and immobility of the diaphragm, determined by physical signs and by roentgenoscopic examination, with pain over the apex of the shoulder.

Diaphragmatitis must be differentiated from spontaneous pneumothorax, artificial or spontaneous pneumoperitoneum, acute conditions of the abdomen which extend to the diaphragm or the transversus abdominis muscle, intercostal herpes zoster, pleurodynia, acute spasm of the diaphragm, irritation of the phrenic nerve in the mediastinum, basal pneumonitis, scalenus syndrome, and cervical ribs.

There is no specific treatment for this condition.

Epidemic Hiccough (Devil's Grippe). Epidemic hiccough has been observed in rural communities The consensus is that the disease is due to an infection of viral origin. The causative organism is unknown. The infection apparently spreads through families by contact.

The onset is sudden, with epigastric and thoracic pain and increased respiratory rate. *Respiration may be difficult, and in some cases the rate is as high as 60 per minute* From the onset there is often a fever, with the temperature from 101 to 105 F (38.3 to 40 5 C). Profuse perspiration is the rule There may be nausea and vomiting in the early stages of the disease. After about 4 hours of severe paroxysms of pain and dyspnea the symptoms subside. In no case do severe symptoms persist more than 24 hours without relief After 3 or 4 days from the onset *there may be* diarrhea.

Examination of those who have paroxysms of abdominal pain may reveal muscle guarding and splinting In all others the presence of hiccough is the only positive finding

The diagnosis in a sporadic instance of the disease cannot be made. Diagnosis is established during an epidemic mainly by the short duration of the hiccough, fever and the presence of other cases in the community.

The differentiation of hiccough from diaphragmatic tic is made on the rate of diaphragmatic activity *Hiccough may occur at rates of from 10 to 20 times per minute.* In the diaphragmatic tic or spasm which follows encephalitis the contractures occur from 60 to 200 times per minute. In diaphragmatic tic roentgenoscopic inspection of the diaphragm reveals these contractions with no other movement. On forced respiration, however, the diaphragm is seen to descend and ascend while the small, rapid contractions continue. In some cases temporary or *permanent* interruption of the phrenic nerve has been necessary.

In ordinary hiccough no effective treatment is known which deserves mention. Inhalation of oxygen and carbon dioxide, if administered by the use of a mask, prevents the patient from uttering audible complaints.

Trichinella Spiralis. *Trichinella*, a genus of the nematode parasites of the family Trichinellidae, causes the disease trichinosis, and may cause a primary diaphragmatitis. The organisms enter the diaphragm, as is true of other muscles of the body, and may produce serious myositis Indeed, the involvement, together with that of the intercostal muscles, may become so *extensive as to cause death* (see Intestinal Parasites, Chapter 13).

bowel, the mortality is high immediately following the accident. After the acute injury has improved surgical operation may not be immediately urgent.

DISEASES OF THE DIAPHRAGM SECONDARY TO DISTURBANCES OF INNERVATION OR PSYCHIC CONTROL

Paralysis of the Diaphragm. Unilateral or bilateral paralysis of the diaphragm may be caused by hemorrhages, poliomyelitis, and tumors involving the spinal cord or the phrenic nerve Injuries or operations on the neck may crush or disrupt the phrenic nerve and thus result in temporary or permanent diaphragmatic paralysis on the same side Injury of the brachial plexus may cause paralysis of the diaphragm A tuberculous process or malignant lymphoma adjacent to the phrenic *nerve, as it courses through the thorax, may involve it so as to result in paralysis* of the diaphragm.

When the entire diaphragm is paralyzed, excitement or exertion results in marked dyspnea In unilateral paralysis symptoms are meager or absent In those who have extensive adhesions in the upper part of the abdomen, severe motor symptoms referable to the intestines may follow interruption of the phrenic nerve, and subsequent diaphragmatic paralysis may develop, particularly when the interruption is of the left phrenic nerve

On examination in some instances visible paradoxical movements of the diaphragm are observed When one side of the diaphragm moves downward while the other side moves upward on inspiration, paralysis is suspected.

In most instances the diagnosis is made by roentgenoscopic examination

There is no treatment capable of restoring the function of the paralyzed diaphragm

Spasm of the Diaphragm (Hiccough, Hiccup, Singultus). Hiccough is a sudden contraction of the diaphragm. If the mouth is not kept closed during the singultus, a sound is produced by the quick closure of the glottis Hiccough is often produced by the swallowing of dry food without sufficient drink It is a common postoperative complication, perhaps from an irritation within the abdomen It is an ominous symptom in general peritonitis Pleuritis or pericarditis may cause hiccough Involvement of the phrenic nerve anywhere along its course is a common cause of hiccough Tumors in the medulla, encephalitis, injuries to the phrenic nerve from wounds and trauma, pressure from tumors in the neck or thorax, disease of the meninges or vertebrae in the region of the third and fourth thoracic roots, peripheral neuritis, lead poisoning involving the phrenic nerve, and inflammation of the terminal fibers within the diaphragm may result in hiccough Epidemic hiccough is thought to be associated with encephalitis Sometimes hiccough is a hysterical manifestation

The onset is sudden regardless of the cause There may be only a few contractions of the diaphragm, after which the condition completely disappears When hiccough persists, pain and soreness may be experienced over the attachments of the diaphragm to the thoracic wall and of the muscles of the thorax and abdomen

Hiccough usually is a simple and harmless condition However, if it persists, it may lead to exhaustion and to death. When the diaphragm becomes weak from prolonged hiccough, the bases of the lungs do not fill well with air on inspiration, and congestion results The dangers of bronchitis and pneumonia are then obvious. When prolonged hiccough occurs in persons suffering from terminal diseases, it often indicates that death is near

The diagnosis of hiccough is obvious. A diagnosis of the cause of the symptom hiccough is often impossible. The usual types clear spontaneously.

Diaphragmatic Flutter. Irregular clonic spasm of the diaphragm, or hiccough, is a common disorder in health, and its significance in disease is variable Tonic spasm of the diaphragm is seen in chronic form in emphysematous patients and

Any abdominal suppurative process or abdominal operation followed by an unsatisfactory postoperative course which is characterized by chills, fever, pleural pain and effusion, and unilateral elevation of the diaphragm arouses suspicion of the possibility of a subphrenic abscess.

The most dependable roentgenologic evidence indicative of subphrenic abscess are evidences of pleural effusion and elevated diaphragm. These roentgenologic findings are not conclusive, but *in correlation with the history and the other findings* they are strongly suggestive of subphrenic abscess. In some cases the roentgenologic findings are negative Early diagnosis of subphrenic abscess is usually dependent on a suspicion of its presence Once the diagnosis is suspected, the institution of proper treatment depends on localizing the lesion as accurately as possible to determine the most satisfactory approach for surgical exploration

DISEASES OF THE DIAPHRAGM DUE TO TRAUMA

Traumatic Eventration of the Diaphragm. Traumatic eventration of the diaphragm is designated also traumatic hernia, false hernia and hernia spuria

Eventration of the diaphragm results from a tear in the diaphragm Such tears often are sustained *from blows to the lower part of the thorax or the upper part* of the abdomen; accidents which result in crushing of the thorax, gunshot or stab wounds, or extreme straining In some cases of injury only the muscle is affected, and the peritoneal and pleural coverings of the diaphragm remain intact. Thus, when the abdominal contents enter the thorax, they carry with them the sac and may be considered as true hernias. In other cases the rupture is complete, whereupon the abdominal contents pass into the thorax without a sac The size of the tear determines the degree and severity of the hernia A small rent may become enlarged through pressure on the abdomen or through extreme contraction of the abdominal muscles as in straining As in congenital diaphragmatic hernia, eventration occurs most frequently on the left side However, both right-sided and left-sided rents in the diaphragm occur. When a tear is situated on the right side, a part of the liver itself may extend through the opening

Immediate death may result from the diaphragmatic eventration In the usual patient, however, the initial symptoms have commenced with nausea, vomiting, pain, dyspnea and hiccough. As the patient recovers from the acute illness he has pain in the thorax, often simulating angina pectoris, gallbladder colic or vague chronic digestive disorders The pain, belching and feeling of fullness in the thorax are worse after meals and particularly on retiring at night when the stomach is full

On examination and on inspection soon after the accident, if a large volume of the abdominal contents has entered the thorax, the abdomen appears flat and there may be evidence of recent trauma such as a puncture wound or crushing injury. Movements of the thoracic wall on respiration are markedly restricted

Palpation discloses that the movements of the thoracic wall are markedly decreased or absent on the involved side. Tactile fremitus cannot be elicited and the heart may be displaced toward the contralateral side. The percussion note depends on which part of the abdominal contents has entered the thorax If the spleen has entered or if blood has accumulated, a flat note is elicited If the stomach and intestines are present, a tympanitic note may be heard On auscultation, because of the collapsed or compressed lung, breath sounds are absent and the sounds due to air and fluid in the stomach and intestines usually heard over the abdomen may now be elicited over the thorax After recovery from the immediate effects of the accident examination by physical means may be negative.

Roentgenologic examination after ingestion of a barium meal reveals evidence of parts of the *gastrointestinal organs in the thorax*

Immediate surgical operation may be indicated for the acute injury. Pleurisy and peritonitis are always possible complications Because of shock and strangulated

increase in voice sounds Abscesses in the posterior mediastinum sometimes rupture into the trachea or bronchi, the esophagus or pleural cavity. Occasionally they appear in a posterior triangle of the neck. Those which extend into the retroperitoneal space may manifest themselves in the groin

Abscesses in the posterior mediastinum may disappear soon after drainage is established through rupture into the esophagus, the trachea or a bronchus.

The diagnosis is seldom made until rupture occurs. However, if the condition is suspected, the ingestion of barium sulfate by the patient enables visualization of the esophagus displaced ventrally Often there is evidence of obstruction due to pressure. Abscesses in other mediastinal parts, if they should occur, are not diagnosable

MEDIASTINAL EMPHYSEMA

Air in the mediastinum may follow severe coughing, crying, lifting, straining at stool, thoracic injuries, overdistention of the lungs, surgical procedures on the lungs and pleura, the use of positive-pressure anesthesia, spontaneous interstitial pulmonary emphysema, pulmonary diseases such as bronchopneumonia, influenza, asthma and tuberculosis, and a ruptured abdominal viscus

On reaching the mediastinum, air travels along courses of least resistance toward the cervical, occasionally toward the abdominal regions In the neck air localizes in the subcutaneous tissues where it is detected by means of the crepitations elicited on palpation The air reaching the retroperitoneal space may rupture through the peritoneum and result in pneumoperitoneum, or it may course downward through the inguinal rings, causing subcutaneous emphysema of the thighs and abdominal wall Air in the peritoneal cavity, when there is no rupture of an abdominal viscus, usually arrives there from the lungs

Symptoms. Often the escape of air into the retroperitoneal space and into the region of the neck is accomplished with but mild discomfort However, if air reaches the mediastinum under high pressure, as for instance from a high pressure pneumothorax, the pain is excruciating The pain may extend to the left shoulder and the left arm There is a sense of pressure beneath the sternum Swallowing and turning the head are painful There are severe dyspnea and cyanosis When the intramediastinal pressure approaches zero, the return flow of blood to the auricles is lessened through compression of the systemic and pulmonary veins

Examination There is often swelling of the cervical region when the subcutaneous emphysema is marked The presence of swelling over the abdomen, the inguinal region, and the thighs may signify subcutaneous emphysema in these regions

A subcutaneous emphysema is characterized by crepitations on palpation of the subcutaneous tissue When considerable air has accumulated in the mediastinum, the percussion note over the sternum becomes hyperresonant On auscultation, crackling, popping sounds are heard over the sternum and over the surface of the neck and along its borders which are increased when the heart is in systole

Diagnosis The physical findings are diagnostic. In instances in which diagnostic uncertainties prevail, lateral roentgenograms may be very helpful

Usually the prognosis is excellent. In most cases of mediastinal emphysema treatment is not required

In instances of acute mediastinal emphysema the syndrome of acute coronary occlusion may be simulated A short period of observation plus electrocardiographic studies will identify the condition present.

TUMORS OF THE MEDIASTINUM

Infections may reach the mediastinal lymph nodes from the neck, the abdomen, the lungs and pleura and the surface of the thorax and cause them to enlarge. The tubercle bacillus is the chief cause of the enlargement, but other agents also, such

cannot be made by any means of examination. It is suspected if the infection extends to the neck or downward into the retroperitoneal tissues or into the hili of the lungs

Acute Mediastinal Abscess. The etiology of acute mediastinal abscesses is the same as that of acute mediastinitis. Abscesses in the anterior mediastinum are caused by extensions of infection from lymph nodes, and by erysipelas, and occur after operations on the lungs, the larynx, the neck and the sternum. Occasionally a mediastinal abscess is a complication of disease in the abdomen, for instance, a gallbladder infection, and particularly perforation of the gallbladder.

There is moderate fever, and pain and throbbing are present beneath the sternum. The pain is accentuated by movements of the trachea, as by coughing.

On examination, often the veins of the neck are distended. There are swelling and edema of the neck and thoracic wall Increased percussion dullness is often elicited over the manubrium Leukocytosis is present.

The diagnosis may be obvious from the foregoing physical findings in association with roentgenologic evidence of a mass displacing the trachea. At times, if there should be only miliary abscess, the diagnosis may not even be suspected clinically.

Chronic Mediastinitis. Chronic mediastinitis is caused by pyogenic infections, rheumatic fever, syphilis and tuberculosis Unusual causes of chronic mediastinitis are actinomycosis or streptotricosis, pneumoconiosis and chronic paragonimiasis. The following general statements can be made in regard to chronic mediastinitis. (1) The chronic lesions produce fibrosis, which may constrict the innominate veins or the superior vena cava Edema of the face, neck and upper extremities and the appearance of collateral circulation ensues. (2) If the infection extends to and involves the pericardium, there are edema of the feet and legs, ascites, dyspnea, cyanosis and cough (3) If collateral circulation is established, there are enlarged superficial veins over the thorax and abdomen As the scarring tightens, stenosis of the trachea or bronchi ensues which may be evident symptomatically and on roentgenologic examination Paralysis of the recurrent laryngeal nerves is manifested by changes or loss of voice

The roentgenologic examination confirms the symptoms and the physical findings by revealing a dense shadow which protrudes laterally, slightly beyond the costosternal borders Such a roentgenologic finding is diagnostic unless accompanied by a history and the presence of a known disease which could cause a mediastinal fibrosis or tumor.

Chronic Mediastinal Abscess. ***Chronic Abscess of the Anterior Mediastinum.*** Chronic abscesses in the anterior mediastinum may be caused by tuberculosis, syphilis, actinomycosis and infected mediastinal dermoid cyst If there should be symptoms, they result from the primary disease, for these abscesses are usually without manifestations of their own

Percussion directly over the abscess yields dullness and often tenderness This is the only finding on physical examination suggestive of abscess in the anterior mediastinum The findings on percussion, when taken in conjunction with the history and the results of roentgenologic examination, may be diagnostically conclusive

Chronic Abscess of the Posterior Mediastinum. An abscess of the posterior mediastinum may be caused by perforation of the esophagus, or by extension of infection from osteomyelitis of a vertebra, or from infection in the retropharynx, the lung, pleura or abdominal cavity. Occasionally an abscess may arise in situ from diseased mediastinal lymph nodes

The first symptoms are those of pressure. There are pain, dysphagia, cough and dyspnea The pain is increased by swallowing or coughing It is situated between the scapulae and often extends around toward the front of the thorax The abscess may rupture into a bronchus with expectoration of pus Esophageal rupture creates a serious condition

On physical examination there may be dullness over the spinal column with

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as infectious mononucleosis, syphilis, Hodgkin's disease, sarcoma, sarcoidosis and carcinoma, cause enlargement of these nodes.

In children a lobe of the thymus protrudes laterally so as to cast a roentgenologic shadow which may resemble that present in disease of the upper pulmonary lobe. Tumors of the thymus or persistent thymus may be revealed by roentgenoscopic examination

Likewise the thyroid gland may extend substernally into the thorax and result in pressure on the trachea, esophagus, internal jugular vein, carotid artery and the recurrent laryngeal and cervical sympathetic nerves.

Cysts of the mediastinum may be congenital, inflammatory or parasitic in origin. The common tumors of the mediastinum are congenital, namely, dermoid or teratoma, cystic lymphangioma, pericardial celomic cyst, bronchial cyst, gastric cyst, and enteric cyst.

Benign tumors as well as malignant growths often result in pressure symptoms.

SYMPTOMS. Tumors of the mediastinal structures are manifested by symptoms referable to the circulatory system, the respiratory system, the mediastinal nerves, and the digestive system These symptoms are very much the same whether produced by a benign or a malignant growth since they originate largely from pressure of the enlarging tumor

Circulatory Symptoms. When obstruction of the superior vena cava is present, the patient, on arising after stooping or flexing the body, for a minute or two has cyanosis of the face, neck and upper part of the thorax. The superficial veins of these regions become more dilated and engorged than those of a normal person who performs a similar act The engorgement of the face in cases of mediastinal pressure will remain for some time, in contrast to the rapidity with which this flushing will disappear in the normal person In instances of marked obstruction the face may be a bluish black, markedly bloated, and the eyes may bulge as is seen in strangulation Venous obstruction may produce cerebral congestion resulting in dizziness, tinnitus, headache and even loss of consciousness Instances of unilateral venous obstruction often can be demonstrated by having the patient raise both arms to a horizontal position above the level of the upper limits of the heart chambers If unilateral obstruction should be present, the superficial veins of one arm will become distended and remain so while the arm is maintained in the horizontal position

Respiratory Symptoms. A patient who has mediastinal pressure producing respiratory symptoms has dyspnea and cough. The dyspnea at first appears on exertion As the pressure increases, it is paroxysmal or continuous

In the beginning the cough is dry Later, when sputum appears, it is mucoid and finally it becomes mucopurulent, and hemoptysis is common The cough and expectoration result from pressure and obstruction of the air passages, and thus from an obstructive bronchitis.

Respiratory symptoms may be due to traction or pressure on the trachea or large bronchi, or to circulatory obstruction Respiratory stridor and wheezing result from pressure causing narrowing of the trachea or bronchi. Occasionally these symptoms are associated with involvement of the recurrent laryngeal nerve.

Gastrointestinal Symptoms. Vomiting, dysphagia and a sense of strangulation are induced by direct esophageal pressure or irritation of the recurrent laryngeal nerve.

Symptoms of Involvement of Mediastinal Nerves A patient who has a mediastinal tumor which is irritating the recurrent laryngeal nerves has hoarseness or complete aphonia There may be the brassy type of cough formerly considered characteristic of an aneurysm of the aorta

As the result of pressure on the sympathetic nerves, constriction of the pupil on the affected side is frequently an early manifestation. Pressure on a sympathetic nerve may be manifested by unilateral sweating and flushing of the face Vagus

pressure resulting in a slow pulse and hiccough from phrenic nerve involvement is rare but does occur.

A dull aching pain is usually an early symptom Paroxysms of intense pain or a prolonged period of excruciating type of pain may be witnessed. There is a sense of oppression or substernal tightness Pressure on the intercostal nerves may result in neuralgia or neuritis and herpes zoster Pleuritic pain is frequent. Erosion of the vertebrae or the sternum produces the boring pain which occurs so often at night in all bone diseases

EXAMINATION On examination there may be observed exophthalmos, and dilatation, contraction or inequality of the pupils. Edema, cyanosis or unilateral flushing and perspiration of the face may be apparent. There is dyspnea on exertion early in the disease If dyspnea should be well established on slight exertion or while at rest, orthopnea is present

A slight fullness of the intercostal spaces near the sternum or a bulging of the sternum in the midline is usually present in dyspneic patients. A nonexpansile pulsation of the bulging region is likewise often observed. The tumor may be visible in the sternal notch or above the sternoclavicular articulation If the mediastinal involvement results from a tumor which arose in the neck, this fact is obvious

. Evidences of interference with the circulatory organs are manifested late in the disease There is usually unilateral dilatation of the veins of the thorax, neck and occasionally the face. The jugular veins are prominent and the veins between the clavicle and the third or the fourth rib anteriorly are distended and tortuous. Occasionally the distended and tortuous veins can be seen on the back below the diaphragm Local cyanosis and edema corresponding in area with the venous dilatation are constantly present

The neck, the sternal notch and the axilla are palpated to determine the presence of tumors or enlarged lymph nodes Enlarged nodes may be felt in the axilla, in the supraclavicular region, or along the lower border of the pectoral muscle. Palpation may reveal deviation and fixation of the larynx and trachea A tracheal tug is more frequently associated with an aortic aneurysm but it may be present in other mediastinal tumors There is often a decreased expansion of the thorax The pulse may be slow from vagal irritation or fast from a weak heart Inequality of the two radial pulses from unilateral interference with the arterial circulation is often present.

Submanubrial dullness may be elicited on percussion This dullness rarely can be demonstrated, however, unless it extends beyond the sternal edge. The area of dullness is often irregular in outline and extensive In some posterior tumors, percussion over the thoracic spines may demonstrate an abnormal flatness to percussion, unless the tumor is large, however, there will be no definite dullness on percussion. In large tumors there is decreased or absent vocal fremitus over the area of percussion dullness

On auscultation, in some instances of large tumors, there is an increased transmission of tracheal respiration in the dull area over the manubrium and absent or diminished transmission of voice or breath sounds over other areas. If there should be pressure on a main bronchus, respiratory sounds on one whole side of the thorax may be suppressed or absent Medium, coarse, piping or musical rales may be heard in one or both lungs as a result of pressure of bronchitis

DIAGNOSIS. The presence of manifestations of mediastinal pressure which affects the mediastinal circulation, respiration, or nerves singly or in combination is clinically unmistakable The nature of the tumor, as to whether it is benign, malignant or of vascular origin (aneurysm), can often be determined by the roentgenologist.

Teratomas and dermoid cysts occur behind the sternum, rarely in the posterior mediastinum, in patients less than 30 years of age. Difficulty in diagnosis of these follows perforation into a bronchus with the ensuing infection.

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Inspection does not reveal abnormalities On first palpation and percussion there are no abnormal signs By the time the sputum begins to be profuse and to collect in the bronchial tubes, vibrations produced by it on breathing may be felt on the surface of the thoracic wall. On auscultation there are sibilant sonorous bronchial rales Later, coarse, moist and bubbling rales are heard. Coughing may result in a temporary disappearance of rales. The breath sounds may be masked by the numerous rales throughout the thorax The physical signs in acute bronchitis are usually elicited equally well over both sides of the thorax When the physical signs are encountered over only a part of one lung, the condition therein is a more serious condition than acute bronchitis

Diagnosis is established by physical examination Acute bronchitis may be a serious disease in infants and elderly persons, especially in those who have emphysema, asthma or heart disease In otherwise normal persons recovery is the rule Occasionally an acute bronchitis progresses and pneumonia develops

Acute Bronchiolitis (Capillary Bronchitis). An acute inflammation, mainly of the walls of the bronchioles, is caused by bacteria and probably viruses The first symptoms are often those of an acute respiratory infection The symptoms become more severe and soon dyspnea and then cyanosis develop The temperature rises to 103 or 104 F (39 4 or 40 C). The cough is distressing Moderate prostration ensues.

The patient appears to be seriously ill There are cyanosis, profuse perspiration, shallow and rapid breathing Findings on palpation and percussion are normal throughout the lungs Auscultation reveals early in the course of the disease sibilant rales and, later, fine, moist rales throughout the lungs

Cultures of the sputum reveal a preponderance either of the influenza bacillus or of the hemolytic streptococcus [illegible]

The results of roentgenologic examination likewise are indefinite This condition simulates a diffuse bronchial pneumonia If the course is favorable, the diagnosis may not be made, otherwise the diagnosis awaits necropsy

Oxygen, chemotherapy or antibiotics are desirable

Chronic Bronchitis. Chronic bronchitis in adults occurs in those debilitated by tuberculosis, emphysema, circulatory insufficiency, bronchiectasis, allergic conditions, infection of the paranasal sinuses, pneumoconiosis, fungous infections, fusospirochetal infections, foreign bodies, dust and benign or malignant tumors The aged are prone to have this disease

The cough is constantly present and tiresome Soon after meals the cough may cause vomiting and thus adds to the weakness and often loss of weight The cough and expectoration are always worse on breathing of cold damp air The muscles of the lower thoracic wall, and particularly those of the upper abdominal wall, may become sore and tender to a degree that an intra-abdominal disease may be suspected

The eyes are often reddened and the lids may be hemorrhagic from the cough. An emphysematous-shaped chest is present. The lungs are hyperresonant on percussion and there are musical rales on auscultation These may clear on deep breathing Medium and fine rales may be elicited over the bases which do not clear on deep breathing The breath sounds may be somewhat diminished and the expiratory phase of respiration is longer and lower pitched than usual On palpation of the upper part of the abdomen there may be diffuse soreness and tenderness of the muscles Palpation and percussion often reveal evidence of primary disease of the circulatory apparatus

The diagnosis is established by a process of elimination of primary disease such as tuberculosis, heart disease, malignant disease, fungous infections and pressure on the trachea or bronchi

Malignant tumors of the thymus may be suspected if there should be the accompanying symptoms of myasthenia gravis. Lymphosarcoma (Hodgkin's type) is usually manifested by involvement of the lymph nodes of the neck before there is manifest mediastinal pressure.

Aneurysms can usually be determined by roentgenoscopic examination.

Invasion of the mediastinum by malignant neoplasms from elsewhere in the body occurs by direct extension or by lymphogenous or hematogenous spread Direct extension to the mediastinum occurs in carcinoma of the trachea, bronchi, esophagus and breast. Carcinoma of the breast may also metastasize by the blood stream or the lymph stream. Lymphatic and blood-stream metastasis to the mediastinum is extremely rare The symptoms and physical findings are evidence of pressure on one or more of the mediastinal contents Diagnosis usually depends on recognition of the primary tumor

Except for secondary invasion of mediastinal structures by sarcomatous growths, sarcoma is rare. Metastatic involvement of the mediastinum from axillary melanosarcoma and bone sarcoma has been reported. Besides the signs and symptoms of the primary growth, those of pressure or invasion of mediastinal structures may be found.

DISEASES OF THE BRONCHI

The Bronchial System. The *right main bronchus* is larger than the left and is more nearly a continuation of the trachea The right main bronchus divides into the right upper, the middle, the dorsal and lower branches

The *right upper lobe bronchus* divides into three segmental branches (1) right anterolateral segment, (2) right posterolateral segment, and (3) right apical segment.

The *right middle lobe bronchus* divides into two major branches, one of which supplies the right anterior middle segment and the other supplies the right lateral middle segment of the lung

The *dorsal bronchus* divides into the anterior, posterior and middle bronchi which supply lower lobes of the lung

The *lower branch* divides twice into the mid, posterior and anterior basic branches

The *left main bronchus* is immediately more branching in character than the right main bronchus The first division of the left main bronchus divides into the left upper lobe bronchus, the anterolateral, the lateral mid, anterior mid, anterior basic, mid basic, posterior basic and dorsal bronchi

The Bronchi and Lungs as Originators of Pain. Clinically, according to Jackson, pain is almost never noted during bronchoscopic manipulations, even in dealing with sharp-pointed foreign objects which inevitably inflict some trauma Occasionally a patient with a bronchial foreign body is able to localize it correctly as to side. Real pain is extremely rare in these cases unless there is pleural involvement Pain does appear to be felt more in the bronchi than in the trachea, but possibly this is due to the proximity to the pleura

Acute Bronchitis. Acute bronchitis is usually a part of a catarrhal inflammation of the bronchi, trachea and larynx It frequently begins as an acute infection of the respiratory tract.

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tion in the throat and beneath the sternum may be distressing From 1 to 2 days after the onset the sputum may become profuse *Quantities of yellowish* greenish stringy mucous material, sometimes with a fetid odor and often blood streaked, may be expectorated. In some instances the onset may be with fever (temperature 100 to 101 F, or 37.8 to 38 3 C). There is generalized aching, particularly severe over the lumbar region and down the legs Except in those who have asthma and chronic conditions of the bronchial tree, the symptoms pass in 3 to 5 days

The age and sex of the patients fail to show marked differences in the types of the disease. Blood-spitting is commoner with saccular dilatation than with other types. In Chapman and Wiggins' series of cases blood-spitting had occurred in 42 per cent for more than 2 years About one half estimated the amount at 1 ounce (30 ml) or less in 24 hours About 40 per cent were unaware of having had pneumonia. The incidence of pneumonia in saccular bronchiectasis was greater than in the cylindric type. Influenza if present was unknown to 27 per cent. There was no significant difference in its incidence among the three types. Nasal disease was a complaint of 35 per cent Its incidence was about the same in the three types. Physical signs were absent more often in cylindric bronchiectasis than in the other types The only patients known to have asthma were in the cylindric group. These data on the distribution of the disease differ in that there was a relatively higher incidence in the right lower lobe as compared with the left. This is unexpected in view of the fact that congenital bronchiectasis should involve the left lower lobe more commonly It appears that distinction between cylindric and saccular bronchiectasis is based on sound statistical grounds This is not the case with other morphologic types

In advanced disease extensive fibrosis, emphysema and cavities are present. Occasionally an abscess may appear in a part of the lung not involved by bronchiectasis as the result of aspiration of infected material from the involved bronchi.

In the so-called dry type of bronchiectasis the parenchymal changes are slight, but in some patients the fibrosis continues to develop until it extends throughout the lung or lungs As the fibrosis progresses, compensatory emphysema obscures the physical signs of the disease

There are both congenital and acquired forms of bronchiectasis Regarding the congenital form of bronchiectasis, Olsen stated that the condition in the lungs is manifested in almost half of the cases before the age of 10 years and that it follows an attack of influenza, measles, pertussis or pneumonia. Often there is an associated dextrocardia

Acquired bronchiectasis develops after streptococcal bronchopneumonia either in childhood or in adulthood First the changes involve the bronchial mucosa, the submucosa and the pulmonary parenchyma Progression of these changes results from recurring bronchopneumonia The chronic stasis and infection distal to a bronchial stenosis or obstruction from any cause sequentially induce development of bronchopneumonia, pulmonary abscess and, later, indurative pneumonia and bronchiectasis

Symptoms Small regions of bronchiectasis are often symptomless, but such small regions may be the point of origin of severe hemorrhages In those who have symptoms, paroxysms of coughing when the patient changes position, often soon after getting out of bed in the morning, are common The cough may or may not bring up large quantities of sputum The paroxysms of cough may last from a few minutes to an hour or more

Pulmonary hemorrhage is a common complaint of those who have bronchiectasis Vinson found that in 100 cases of chronic bronchiectasis there were histories of pulmonary hemorrhage in 49 According to Vinson these pulmonary hemorrhages are not predictable on the basis of degrees of involvement of the lung tissues, or of prodromal symptoms

In many instances the patient often has observed that on bending forward while coughing a large amount of sputum is obtained

Examination Inspection reveals widening of the intercostal spaces, retraction and lagging of the thoracic wall, and perhaps the absence of the phrenic wave signs (Litten's sign). Clubbing of the fingers and the toes often appears soon after the onset of the symptoms The clubbing may involve only the soft tissues or may be associated with hypertrophic pulmonary osteoarthropathy. Dyspnea is present when there are advanced pulmonary fibrosis and emphysema.

On palpation tactile fremitus may be increased or normal, depending on the amount of pulmonary fibrosis and its proximity to the periphery of the lungs.

Fibrinous Bronchitis. This form of chronic bronchitis is called also pseudomembranous, membranous croupous, mucinous, and plastic bronchitis.

The etiology of fibrinous bronchitis is not known. The condition, in addition to other symptoms of bronchitis, is characterized by the *expectoration of casts of* fibrinous mucous material The casts have the shape of the bronchial ramification in which they were formed.

In the acute stage of the disease cough, chills and fever are present which are *followed by pain and dyspnea and expectoration of the casts. In the chronic stage* the symptoms are mild but prolonged. Hemoptysis is common after expectoration of the casts.

On examination the findings are those of chronic bronchitis In diagnosis the presence of the casts in the sputum is the only distinguishing feature of this form of chronic bronchitis from all others

Tracheobronchial Tuberculosis. Tracheobronchial tuberculosis is frequent in primary pulmonary tuberculosis of children and adolescents and in the re-infection type of pulmonary tuberculosis in adults

The bronchial mucosa is frequently the seat of both tuberculous and non-tuberculous lesions. The bronchi are either compressed by the enlarged lymph nodes or retracted by sclerosis of the pulmonary lesions. The evolution of tuberculous bronchial lesions runs parallel with the evolution of the tuberculous process in the involved lobe. Acute exudative bronchial tuberculosis appears in some cases years after the regression of the pulmonary tuberculosis and its calcification

The symptoms are often those of an asthmatic or chronic bronchitis. The diagnosis is established by demonstration of tubercle bacilli, and by bronchoscopic and roentgenologic examination followed by histologic and cultural examinations of biopsy tissue

Broncholithiasis (Pneumoliths or Lung Stones). Broncholiths are composed largely of calcium Lung stones may be present in inspissated pus, in regions of tuberculous caseation in lymph nodes and lungs, around aspirated foreign bodies

Broncholiths may develop within the bronchi or may originate outside the *bronchi, with subsequent perforation into the air passages. In the* majority of cases broncholiths are due to perforation of calcified tuberculous lymph nodes into the bronchus The changes found in the presence of broncholiths may simulate carcinoma of the lung, chronic pulmonary abscess, bronchiectasis with atelectasis and *chronic pneumonitis as well as mycotic disease Body section* roentgenography is of diagnostic aid in bronchopulmonary lithiasis

The clinical symptoms may vary from complete absence of signs or symptoms to those of a severe or critical illness Practically every pathologic condition which *may develop in the thorax may be simulated. Bronchopulmonary* lithiasis should be included in differential diagnosis of bronchial obstruction, pulmonary suppura-

of the bronchial wall through which the stone has passed. The diagnosis is not frequently made. The patient expectorates a stone, followed by a small amount of blood and the illness is over without the physician knowing anything about it

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part

of one lobe of either lung, in the base, or the disease may affect bronchi [illegible] iout the greater part of both lungs.

The types of bronchial dilatations by roentgenographic study are the cylindric, saccular, varicose, fusiform and bronchiolectatic; with the cylindric, saccular and varicose forms being the common types.

The age and sex of the patients fail to show marked differences in the types of the disease. Blood-spitting is commoner with saccular dilatation than with other types In Chapman and Wiggins' series of cases blood-spitting had occurred in 42 per cent for more than 2 years. About one half estimated the amount at 1 ounce (30 ml) or less in 24 hours About 40 per cent were unaware of having had pneumonia The incidence of pneumonia in saccular bronchiectasis was greater than in the cylindric type. Influenza if present was unknown to 27 per cent. There was no significant difference in its incidence among the three types. Nasal disease was a complaint of 35 per cent Its incidence was about the same in the three types. Physical signs were absent more often in cylindric bronchiectasis than in the other types. The only patients known to have asthma were in the cylindric group These data on the distribution of the disease differ in that there was a relatively higher incidence in the right lower lobe as compared with the left This is unexpected in view of the fact that congenital bronchiectasis should involve the left lower lobe more commonly It appears that distinction between cylindric and saccular bronchiectasis is based on sound statistical grounds This is not the case with other morphologic types

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Fremitus is decreased if the pleura is thickened. In the presence of emphysema of the lungs, there is a decrease in tactile fremitus

On percussion, changes are present in those who have a thickened pleura and emphysematous regions

The auscultatory findings are often within normal limits. Occasionally there are fine to coarse and intermittent rales, depending on whether or not the contents of the sacculations of the bronchi have been expectorated The breath sounds may be bronchial or cavernous when there are large empty bronchiectatic cavities.

On endoscopic examination there may be discovered a foreign body or some other obstruction, the removal of which, if feasible, facilitates treatment or cures the patient.

With the head and shoulders nearly to the floor, forced coughing will often be followed by the expectoration of a large amount of sputum Within a 24 hour period a volume of sputum equaling 2 pints (1 liter) or more may be expectorated. The sputum is often blood streaked and in it are greenish yellow masses ½ inch to 1 inch (1.27 to 2.5 cm) in diameter (Traube's or Dittrich's plugs). When allowed to stand, the sputum separates into three layers The bottom layer is opaque with pus, cellular debris, bacteria and occasionally elastic fibers, the middle layer appears somewhat clear and watery, and the top layer is frothy. The sputum is examined for tubercle bacilli since tuberculosis may coexist with or be the cause of bronchiectasis

Diagnosis The diagnosis is suspected from the history and is confirmed on the examination Usually the pulmonary involvement is detected on roentgenologic examination An endoscopic examination is often invaluable in detection of a localized bronchial stenosis or of a foreign body obstructing a bronchus

Postural drainage should be instituted at once The surgical removal of the involved lobe, or even the entire lung when necessary, is satisfactory if the patient survives the operation and the patient is not left with an incapacitating postoperative thoracic pain

Bronchostenosis. Bronchostenosis may develop from pressure extrinsic to a bronchus or from inflammation or growths from within its walls Conditions which cause bronchostenosis also cause bronchial occlusion. Prickman and Moersch examined endoscopically 140 patients suffering from asthma, in 60 of whom definite stenosis was found in one or more bronchi

A significant and prominent symptom is severe, persistent and sometimes paroxysmal cough, often of long duration and dating from an acute respiratory infection At times it may be impossible for the patient to cough up the sputum Then at times the cough loosens and there is profuse, mucopurulent sputum streaked with blood This increased amount of sputum represents some of the secretions which have been retained by the stenosis Bronchostenosis may result in pneumonitis and atelectasis and if not relieved, bronchiectasis may ensue

The physical signs are those of pneumonitis and atelectasis Often a wheeze is elicited, and occasionally crepitant rales are heard.

A presumptive diagnosis of bronchostenosis is often made from the history and physical findings The exact diagnosis is made only by the bronchoscopist or the roentgenologist

Bronchial Perforation. Acute or chronic pyogenic abscesses, chronically inflamed lymph nodes containing lung stones, and lesions of chronic pulmonary tuberculosis may perforate ramifications of bronchi and discharge their contents into the bronchial system. Materials thus discharged are distributed peripherally, and in the case of tuberculous material acute pulmonary tuberculosis may ensue

The symptoms are those of the prevailing disease.

Results of examination often are negative In some instances tubercle bacilli may be found in the sputum or gastric washings although the lungs appear entirely clear on examination

The diagnosis is made by a capable bronchoscopist

Bronchial Fistulas. Bronchial fistulas are often the sequence of perforations of the viscera of the abdominal cavity After perforation of abdominal viscera a subphrenic abscess forms with subsequent perforation of the diaphragm and into a bronchus. In the course of empyema or subphrenic abscess bronchocolic fistula may develop.

The symptoms are obscured by those of subphrenic abscess

The diagnosis is often difficult; however, Escherichia coli found in abundance in the sputum or an abundance of pus in the feces is suggestive. Bronchography may suffice if the iodized oil enters the fistulous tract and empties into the colon. If this method fails, a barium enema may be helpful if the barium enters the bronchial system When the fistula fails to close, surgical treatment may be indicated.

Bronchobiliary Fistulas. Bronchobiliary fistulas develop when hepatic abscesses penetrate the diaphragm and a communication is established with one of the larger bronchi Common causes are amebic and echinococcal infections of the liver The sequence of events in an occasional case is the formation of gallstones followed by suppurative cholangitis with perforation, and formation of a small subphrenic abscess with perforation of the diaphragm and a bronchial ramification.

The diagnosis can be made when the patient expectorates bile. In some cases roentgenologic examination following the administration of iodized oil reveals the fistulous tract When such fistulas do not close, surgical intervention may be considered

Broncho-esophageal fistulas are usually fatal However, an occasional patient is observed who has a fistula which has slowly developed as the result of some chronic disease in the esophagus or in a bronchus who has lived for a long time In rare instances broncho-esophageal fistula has followed pneumonia and the patient may have lived for a long time on very low fluid intake to avoid coughing when liquids were swallowed

The symptoms of a broncho-esophageal fistula are cough and dysphagia immediately after swallowing food or drink unless the liquid is taken in sips Paroxysmal half-vomiting and half-coughing characterize this type of dysphagia

It is important to determine the general physical condition and to discover evidence of the underlying disease There are no physical signs indicative of these fistulas

If one of these fistulas is suspected, endoscopic examination of the esophagus is diagnostic.

Bronchial Obstructions and Pulmonary Atelectasis. Xalabarder defined atelectasis as the absence of air in the pulmonary alveoli with intense retraction and shrinking, the latter differentiating it from simple pulmonary collapse. As a result of the vascular dilatation characteristic of atelectasis intra-alveolar exudates from simple serous edema to hemorrhagic suffusions are produced Reversion is likely to occur, but if inflammation persists a long time a progressive fibrosis prevails The mechanisms of the production of atelectasis are not always obvious, for (1) there are bronchial obstructions without atelectasis, (2) the existence of bronchial plugs is not constant, (3) atelectasis can be produced by obstruction of a main bronchus but not of a secondary bronchus, and (4) once the gaseous pressure on each side of the alveolar wall has become equal, the alveolus will be relaxed to the maximal limit which its elastic structure permits

Xalabarder has expressed the belief that atelectasis is produced by pulmonary contraction and that it originates from several causes acting on a specially predisposed organ One of these causes may be bronchial obstruction, but this is not an indispensable factor Atelectasis is the abnormal exaggeration of the physiologic pulmonary tone This defective function is of importance in the genesis of other pulmonary phenomena including the active dilatation of the lung (insatiable pneumothorax and functional emphysema) Xalabarder accepted the existence of muscular fibers in the alveolar walls and saw in the functioning of these muscular plexuses,

under regulation by the autonomic nervous system, the solution to a regional contracture in the affected pulmonary zone, that is to say, to atelectasis.

Congenital Pulmonary Atelectasis. Respiratory movements take place during the second half of intra-uterine life, and thus some of the intrapulmonary spaces are occupied by amniotic fluid This fluid may cause changes in the lungs which prevent full expansion of the lungs at birth. A failure on the part of the lung to expand may also be due to the congenital absence of alveoli, to bronchial atresia or to obstruction of bronchi.

A widespread atelectasis may prevent breathing by the newborn child In the lungs of the newborn there may be regions of atelectasis which are permanent and which do not cause symptoms These regions of the lung are sealed off and leave only a strand of fibrous tissue When regions of the lung thus degenerate fully, symptoms never occur.

In the lungs of some adolescents and adults there is a well-established bronchiectasis which has been present since early childhood without inflammation of the lungs These regions represent the so-called dry bronchiectasis which may be discovered during life or may be found at the time of postmortem examination. The regions are often situated in the lower lobe of the left lung In other instances these regions may become infected and the manifestations of atelectasis ensue

Obstructive or Acquired Pulmonary Atelectasis. Normally the bronchi are filled with air and the right amount of secretion. The secretion from the bronchi is drained upward This upward drainage is afforded by the pumping effect of respiration, aided by the upward transportation of small particulate matter by the ciliary activity of the cells lining the bronchi, and finally by the expulsive force of a cough

When a mechanical obstruction develops, its effects depend on its degree, on whether the obstruction is complete or partial, and if partial, on whether it is fixed or movable

Complete bronchial obstruction is immediately followed by absorption of gases and total retraction of the involved part of the lungs There may still remain functioning pulmonary tissue in the region of the obstruction which is supplied by a bronchus tributary to the obstructed bronchus Inflammation or edema interferes with absorption of gas and retraction For instance, a lobe of the lung that is distal to complete obstruction by a foreign body may show evidence of atelectasis, edema and inflammatory infiltration, but owing to an anastomosing communication between the alveoli of each lobe it remains partially or wholly distended These communications between the lobes of the lung are a protection against atelectasis that follows occlusion of the smaller bronchi

Pulmonary atelectasis occurs when there is compression of pulmonary tissue or an obstruction to a bronchus. In either case the lung is unable to expand on inspiration There are several conditions which reduce the size of the thoracic cavity sufficiently to produce atelectasis, for instance fluid or air in the pleura, removal of ribs, or paralysis of the diaphragm Under these circumstances the lungs are forced to adjust themselves to the new volume by retraction Lesions of the central nervous system that cause paralysis of the muscles of inspiration are followed by atelectasis

An obstruction of a bronchus, with subsequent retraction of the lung after the air has been absorbed from it, is a common cause of segmental atelectasis.

Postoperative Atelectasis (*Postoperative Pneumonia*). During and after surgical operations, because of pain and sedation the respirations become shallow, the cough reflex is suppressed and there is an immobilization of the thorax in a fixed posture As the result of these abnormal conditions, aspiration and stagnation of secretion from the upper part of the respiratory tract ensue and often atelectasis supervenes The condition in the lung may remain atelectatic or may become pneumonic. Thus the postoperative atelectasis is often a postoperative pneumonia

Postoperative pulmonary obstruction and consequent atelectasis or pneumonia are commoner when acute respiratory infection is present at the time of operation, or when the patient has been exposed to any acute respiratory infection just prior to operation

From one to four days after the operation, if the patient is mentally alert, there

is a feeling of tightness or constriction in the lower part of the thorax, manifested as an oppression during breathing. In extensive involvement there are dyspnea, cyanosis, cough and expectoration. In all, however, whether there are complaints or not during the first three or four postoperative days, the temperature rises to 101 F (38.3 C) or higher The pulse rate will be fast (120 or more).

In mild illness, temperature and pulse rate return to normal within a week. The pulse rate returns to normal before the fever subsides

In many patients the illness is prolonged and there is pneumonitis, or pneumonia finally terminating in bronchiectasis or death

On examination, when feasible, there may be relative dullness to percussion, enfeebled breath sounds, and fine rales over the lower lobe or lobes Bronchial breathing is often present On occasion a pleural rub may be heard. There is retraction of the intercostal spaces during inspiration The diaphragm is elevated and the apex beat of the heart may be shifted toward the involved side

The diagnosis depends on the history, postoperative course, physical findings and results of roentgenologic examinations It is inadvisable to examine very ill patients physically and, in some cases, roentgenologically

Infection Atelectasis. During the course of respiratory infections degrees of atelectasis are often present The small atelectatic portions of the pulmonary tissue assume normal volume and function as soon as the infection subsides Larger regions, resulting from obstruction of larger bronchi, become clinically manifested Long after a bad cold has passed, a cough and expectoration persist which may be indicative of an unknown atelectasis

During the course of an acute respiratory infection there is acute thoracic pain which is situated in the base of the lung beneath the scapula around to the axillary line, and dyspnea, which, if severe, is accompanied by cyanosis When these symptoms are present, the occlusion is large and there is a virulent infection Under these conditions fever and sometimes chills develop.

On physical examination there is elevation of the diaphragm and shifting of the *mediastinum Over the atelectatic portions of the lung there are altered or absent* breath sounds, rales and varying degrees of consolidation

The history, the physical findings and the findings on roentgenoscopic examination are diagnostic These patients should have an endoscopic examination

Alveolar and Pulmonary Adenomatosis. Benign pulmonary adenomatosis is a disease with multiple involvement of the lungs by a process in which the alveoli are filled with distended columnar cells The similarity between this adenomatous process and the metastasizing alveolar cell tumor is sufficiently close to suggest that pulmonary adenomatosis is a potentially malignant tumor. However, extrapulmonary metastasis is unknown in adenomatosis

Pulmonary adenomatosis may have a possible relation to jagziekte, an epizootic pulmonary adenomatosis of sheep, which is considered to be a viral infection. Like pulmonary adenomatosis, metastasis does not occur in jagziekte The attempts to transmit the condition to animals from material obtained from human beings with pulmonary adenomatosis have failed

The sex incidence is two women to one man. The age of the patients has ranged from 30 to 80 years

The symptoms commence with cough which varies from nonproductive and mild to produc[illegible]
dyspnea, [illegible]
followed [illegible]
process, dyspnea can appear very early and be out of proportion to cough and expectoration

Sputum is profuse, frothy, tenacious, and there is difficulty in expectorating it, despite the fact that there is constant welling up of the material into the throat The

absence of hemoptysis and the presence of frothy tenacious sputum appear to be characteristic features of this disease.

Despite the severe coughing and the expectoration of large quantities of sputum, and the severe dyspnea, a good general physical condition may be maintained for several months.

The findings on physical examination depend on the stage of the disease when the examination is made The findings vary from those of a bronchitis through bronchial pneumonia to lobar pneumonia

The diagnosis is based on severe dyspnea and abundant frothy mucoid sputum without blood streaking in a patient who maintains good general condition for several months and then declines Death due to asphyxiation ensues. Roentgenologic examination and microscopic examinations of the sputum are of no specific diagnostic aid To those who are familiar with the appearance of the sputum, which maintains its frothy nature for hours, the diagnosis is tentatively established by this peculiarity Endoscopic examination is rarely helpful diagnostically

MALIGNANT TUMORS OF THE BRONCHI AND LUNGS

Primary Malignant Lesions. *Bronchogenic Carcinoma.* It is thought that there has been a great increase in the number of authentic bronchogenic carcinomas observed in recent years. Eight of every 10 patients who have bronchogenic carcinoma are men With the ladies smoking, many of them excessively, it seems likely that the high incidence of pulmonary cancer in men is not to be accounted for entirely on a possible carcinogenic role of tobacco and cigarette-paper smoke.

Seven or more of every 10 of these neoplasms arise near the tracheal *bifurcation.* The rest arise from the smaller bronchioles and are designated peripheral pulmonary cancers. The peripheral pulmonary cancers vary from small outgrowths of the bronchial mucous membrane to large soft tumors resembling tuberculosis, including cavity formation

Bronchogenic carcinomas arise from the tunica propria or basement membrane On the basis of cellular classification pulmonary carcinomas may give rise to three types of tumors. (1) stratified squamous, (2) adenocarcinoma, and (3) the undifferentiated, basal cell tumors. The stratified squamous cell tumors are more amenable to surgical removal than are tumors of the other types

Metastasis from these tumors occurs by direct extension and passage through the lymphatic structures and the blood stream, and by bronchial embolism Pulmonary tumors often metastasize to the brain

SYMPTOMS The first symptom may be a dry cough, and if the tumor arises in the large bronchi, there are cough, expectoration and hemoptysis. The cough is unproductive, hacking, irritant and persistent. When expectoration begins, it is at first scanty and mucoid in consistency As the disease progresses, the sputum is copious, foul in odor, mucopurulent and streaked with blood Peripherally situated pulmonary cancers cause pain as an early symptom A sudden or an abrupt onset of cough, pain, dyspnea and hemoptysis or hemorrhage may indicate the occlusion of a bronchus. Hemoptysis varies from blood streaked sputum to a distinct but not a profuse hemorrhage

The pain is variable in intensity It may be sharp, dull, aching or lancinating. Continuous and severe thoracic pain in the absence of pleurisy often occurs in cancer of the lung It is always on the same side of the thorax as the growth, but it may be referred to the neck, shoulder, upper part of the abdomen, back, arms or legs.

In the beginning, dyspnea is only exertional It may be accompanied by wheezing or a paroxysm of asthma which continues as orthopnea

Continuous or intermittent fever is almost always present. Emaciation begins early and advances rapidly as fever increases and the disease progresses Cyanosis is late in the course of the disease. It advances rapidly as death approaches.

EXAMINATION The physical findings in carcinoma of the lung vary with the location, size and rate of growth of the neoplasm. Often there are no abnormalities on examination by physical means until there are coexistent pathologic change and complications secondary to the tumor. The primary malignant disease may thus be obscured.

In well-advanced cancer of the lung the thoracic movement may be limited or absent The limitation of thoracic movement in the beginning is confined to the affected side but later both sides are affected If a sufficient volume of effusion is present, the intercostal spaces bulge. As the pressure increases in the thorax, the veins of the neck and thoracic wall are distended, and edema of the face, neck or arms is present. On palpation enlarged lymph nodes may be felt in the lower triangles of the neck and in the axilla

When the disease is advanced, tactile fremitus is decreased or absent over the diseased side and often is increased on the normal side. The cardiac impulse may be displaced toward the side of the pulmonary lesion

There are no changes in the percussion sounds until a considerable portion of the pulmonary tissue is hardened by the tumor. Then the percussion sound is dull or flat Dullness is often lateral to the sternum with a normal area between the dull space and the clavicle

Auscultation late in the course of the disease may reveal that breath sounds are enfeebled or absent If the neoplasm partially occludes a bronchus, a high-pitched tubular breathing is heard When a tumor closes a bronchus, collapse of the part of the lung supplied by that bronchus takes place As a consequence the breath sounds are absent and both vocal and tactile fremitus are diminished or absent. Like the other physical signs, the rales, in occurrence and nature, are variable.

DIAGNOSIS If possible, the diagnosis is made before signs are present on physical examination The roentgenologic examination is the most important and can be diagnostically accurate in a large percentage of cases of cancer of the lung. The taking of a roentgenogram after iodized oil has been injected into the bronchial tree is helpful in the diagnosis of some bronchogenic cancers

Conclusive proof of the diagnosis depends on biopsy, which may be accomplished by bronchoscopy The absence of bronchoscopic demonstration of cancer of the lung, however, does not preclude the diagnosis of bronchogenic carcinoma, for the bronchoscope cannot reach all parts of the lung In these patients examinations of the sputum for malignant cells may determine the diagnosis

A diagnosis can often be made from a biopsy of lymph nodes of the neck or axilla or other lymph nodes However, when a diagnosis is thus made, surgical treatment is precluded

Artificial pneumothorax, either alone or combined with thoracoscopy, and exploratory thoracotomy are occasionally required for a diagnosis while the lesion is still circumscribed Justification for these procedures requires an evaluation by successful and experienced specialists

Examination of sputum for cancerous tissue or cells has established the fact that the histologic type of growth can be determined frequently from cells contained in the sputum McDonald observed that the squamous type of cancer cell readily and commonly can be found by appropriate technics The oat-shaped cell type is less frequently demonstrated, and the ciliated columnar or goblet cell type is still less often found The failure to find cancer cells in the sputum does not disprove the diagnosis of carcinoma but is of great diagnostic aid

After the appearance of symptoms, if the lesion cannot be completely excised, the duration of life in most cases of cancer of the lung, other than the squamous cell type, varies from 5 to 9 months. The squamous cell tumors usually progress more slowly

Sarcoma of the Lung. Sarcomas of the lung are relatively rare. A provisional classification of pulmonary sarcomas based on anatomic features has been made by Ewing. These features are as follows: (1) diffuse spindle cell type, (2) large round cell variety, (3) peribronchial sarcoma, and (4) lymphosarcoma.

Sarcomas of the lung are divided clinically into the nodular and the lobar types. The nodular tumors may occur as single or as multiple nodules. In the lobar type a large part of the whole lobe or the whole lung is invaded. Pleural effusion, usually of a hemorrhagic nature, often supervenes.

The symptoms of primary carcinoma and sarcoma of the lung are identical.

Asymmetry of the thorax and dilatation of the veins of the thoracic wall, neck or arm may be present Decreased expansion of the lung involved is often relatively early in its appearance The intercostal spaces may be retracted, or if effusion is present or the growth large, they may bulge.

Palpation confirms the irregularities in expansion. Intercostal tenderness may be elicited in some instances Tactile fremitus is diminished in all surface lesions but normal in the centrally located small growths

In the small nodular growths aberrations of the percussion note may not be apparent In massive invasion of the lung there is a flat percussion note, and definite resistance is encountered by the pleximeter finger. In effusions of more than 500 ml of fluid the percussion note over the fluid and tumor is dull, whereas just above the fluid the skodaic area of hyperresonance is sometimes found

On auscultation the characteristic findings consist of either diminished or absent breath sounds and decreased or absent vocal fremitus. Rales may be present but variable accordingly if atelectasis is present. Rales are constant if caused by congestion or bronchitis

The findings elicited by physical means are never definite enough to form the basis of a diagnosis of either sarcoma or carcinoma of the lung. The roentgenologic examination constitutes the most important diagnostic procedure in cancer of the lung Whether or not the cancer of the lung is carcinoma or sarcoma is a diagnosis to be made by the pathologist. This cannot be determined by either the palpating finger or the roentgenologic examination.

Examination of the sputum for malignant cells is repeated, for this is an important and specific diagnostic test Bronchoscopy is of far less diagnostic value in sarcomas of the lung than it is in bronchogenic carcinoma, for it does not often permit of biopsy because sarcomas are usually extrabronchial.

Aspiration biopsy for obtaining tissue for microscopic diagnosis may be considered after an aspiration of effusion has been done, and examination of the fluid on occasion has not revealed malignant cells Aspiration is rarely advisable

DISEASES OF THE TERMINAL RESPIRATORY PASSAGES AND LUNGS

THE RESPIRATORY PASSAGES

The respiratory passages comprise the nose, the nasopharynx and the pharynx The mouth, the larynx, the esophagus, the two eustachian tubes and the two posterior nares open into the pharynx, which thus serves as the common tract for intake of air, food and drink The diseases of the air passages from the external nares up to the pharynx have been described (pp 85 to 96)

The essential anatomic structures for respiration thus begin with this common tract which is provided by the pharynx and extends inward through the larynx, trachea, bronchi, bronchioles and finally the air spaces (atria) and the supporting tissues of the lungs.

Respiration and Its Control. The lungs are part of a mechanism for insuring that the tissues of the body are adequately supplied with oxygen. The functions of the lungs [illegible] with and inseparable from those of the heart and circulation [illegible] ited and presided over by the

A failure of proper respiration may arise, therefore, from defects in the supply or quality of blood to the lung membrane, from defects in the supply or quality of the air, or from defects in the lungs or of their chemical and nervous control

The respiratory center in the brain extends through the upper part of the medulla oblongata and probably into the pons as well. Although one major and two minor centers have been described, it is well to consider the central gray matter as a whole and to think of it as the respiratory "center" acting as a co-ordinated unit. It possesses an inherent rhythmicity, and it controls the activity of the lower motor neurons supplying the respiratory muscles It receives afferent impulses from the lungs via the vagus nerve, and from the aortic arch and carotid sinus via the sino-aortic nerves It is also influenced by impulses coming from the higher brain centers. It is extremely sensitive to certain chemical variations, for instance the carbon dioxide tension or the hydrogen ion content of the blood, and also to the presence of various poisons such as hydrogen cyanide and carbon bisulfide

Some patients who are of a neurotic temperament and full of complaints may respond, during health or during illness, as a result of certain stimuli, physical or emotional, by overbreathing If this is sufficient to reduce the carbon dioxide concentration in the blood, alkalosis ensues and in its turn may be sufficient to cause an attack of tetany. The attack is due to tissue alkalosis and ends spontaneously, as a result of tissue acidosis consequent on the muscular activity of the tetany. Cessation of overbreathing assists in the return to normal conditions. Alkalosis resulting from spontaneous hyperventilation may cause either tetany or effort syndrome.

Defenses of the Lungs. The inhaled air passes over the upper part of the respiratory tract, where it is warmed and humidified The warmed air is drawn through the larynx, trachea and bronchi into the depths of the lungs, where the interchanges of gases can be made with the blood through the respiratory epithelium

Harmful foreign material from outside cannot easily enter, much less remain in, the lower respiratory passages The microbes present in the air may never reach the trachea A large number of them are trapped in the vestibules of the nose, being enmeshed by the hairs which are moistened with sticky mucus, and later ejected by the action of the ciliated epithelium The ciliated epithelium extends over the walls of the nasal sinuses, the greater part of the nasal cavities, the nasopharynx and the back of the soft palate, trachea and bronchi, as far down as the point where the smallest bronchioles expand into the terminal alveoli Mucus is spread in a thin, even, transparent layer

The larynx protects the lower respiratory passages, when need arises, by its sudden reflex closure Such action is observed on exposure to irritant gases such as chlorine.

Soiled mucus collecting in the interarytenoid region may excite the swallowing reflex, and so help to carry off invading organisms to the stomach, where most of them (but not tubercle bacilli) are killed by the acid secretion If the sensitive larynx, trachea or bronchi are sufficiently irritated, the cough reflex is brought into action, thus foreign material is forcibly expelled, a process aided by the shortening and narrowing of the bronchial tubes which is caused by the forced expiration characteristic of coughing

Organisms passing beyond the larynx are subjected to the mucociliary activity in the trachea and bronchi, some may be carried away by lymphatic drainage, but most will be forced back toward the pharynx.

The trachea and its bronchial branches conduct air from the outside atmosphere to the air sacs of the lungs The larger bronchi divide and subdivide, eventually to become bronchioles, devoid of cartilage and mucous glands, but with a muscular coat relatively twice as thick as that of the larger bronchi Each bronchiole ends in a lobule, enclosed in a fibrous capsule with its own supply of blood vessels, nerves and lymphatics The lobule forms, therefore, a fundamental pulmonary unit, and it is the packing together of innumerable such units which, with the conducting tubes, makes up the lung as a whole Inside the lobule the bronchiole divides into still smaller tubes, the terminal branches of which—the respiratory bronchioles—lead into an expanded space (atrium), each atrium leads into two or three air sacs (infundibula) The air sacs are studded with minute finger-like protrusions, the alveoli, which are lined by a single layer of large flattened cells. The air in these alveoli is separated from the blood capil-

laries only by this single layer of cells and the tenuous walls of the capillaries. The alveoli all over the lung are so packed together that any particular capillary lies between adjacent alveoli, so that the blood is in close contact with air on both sides. In the pulmonary meshwork between the alveoli are large numbers of elastic fibers, nerve fibrils and lymphatic channels.

The terminal bronchioles do not possess ciliated epithelium, so that if microorganisms reach this part of the lung they will be sucked into the air sacs during inspiration, and the only defense left is an inflammatory reaction in the alveolar units This is important in the pathology of pneumococcal pneumonia

CYSTIC DISEASE OF THE LUNGS

Congenital Pulmonary Cysts. Congenital cysts of the lungs exist as solitary and multiple fluid or air cysts Fluid cysts have no communication with the bronchus, air cysts have free communication with the bronchus.

The history often reveals a susceptibility to colds and coughs Dyspnea and cyanosis may have been present from the time of birth If severe respiratory difficulties are observed at the time of birth, congenital cystic disease is probable

SYMPTOMS Often the symptoms are manifested as persistent respiratory discomforts which follow an acute attack of bronchitis, whooping cough or pneumonia There is cough, moderate to severe, with expectoration of mucoid to thick purulent sputum. In the interval between these episodes of symptoms the patient enjoys a comfortable state of health if the cyst or cysts do not communicate with the bronchi If the cysts communicate with the bronchi, there is a valvelike constriction at the point of communication, and sudden serious or even fatal dyspnea may develop, for under such circumstances the essential feature is the same as that of a bronchial fistula from any cause

Spontaneous pneumothorax may occur from rupture of the cyst into the pleural space. In the presence of pneumothorax there follow the sudden paroxysmal, respiratory attacks which are associated with signs of tension pneumothorax. The dyspnea is critical, the cyanosis severe, and each convulsive respiratory struggle seems to represent the last act of the patient Thoracentesis may give temporary relief.

EXAMINATION An examination by physical means may elicit the signs of local tympany or suggest a tension pneumothorax There may be a detectable displacement of mediastinal structures and descent of the diaphragm on the affected side

If a young patient has had staphylococcal pneumonia, a radiolucent region in the lung is most likely an acquired cyst A cystic cavity found before any respiratory illness has occurred suggests a congenital cyst Congenital cysts usually maintain a constant size, while acquired cysts or pneumatoceles tend to fluctuate in size. Congenital cysts may have denser shadows (thicker walls) roentgenographically than acquired cysts Infection in congenital cysts becomes a more frequent occurrence as age increases On thoracoscopic examination the lining of a congenital cyst is smooth and glistening while the wall of a pneumatocele is black. Congenital cysts of the lung persist while acquired cysts tend to disappear spontaneously.

DIAGNOSIS Roentgenoscopic examination aided by means of the opaque media is usually diagnostic The diagnosis is suspected from the history and physical examination

The prognosis is good in fluid-filled or air-containing cysts when not complicated by infection or a one-way valve communication with a bronchus.

INFECTIONS OF THE LUNGS DUE TO BACTERIA

Pneumonia. The conditions necessary for the inception of infection for the production of pneumonia are the implantation of virulent microorganisms or ultramicroscopic life in the terminal airways in sufficient numbers that they cannot be immediately overcome by the defensive forces of the host. An obstructio o drain-

age and local irritation or injury to the terminal airways hastens the inceptive processes

The reactions representing virulence of bacteria and host resistance are complex. Regarding the means of passage of bacteria through the mucous membrane, it is known that the absence of ciliary epithelium in the terminal airways aids the infection to become more easily established, for its normal absence in the ductuli alveolares pulmonis (BNA) permits bacterial stasis in these terminal air units In influenzal pneumonia the ciliated columnar cells so situated in the larger air passages are replaced with cuboidal goblet cells, resulting in the impairment of the capacity of the mucous membranes of the larger air passages to dispose of secretions effectively.

In persons who have had an operation or an injury to the thorax, there are often a disturbance of the cough mechanism and interference with movements of the diaphragm and of the accessory muscles of respiration, and these are major mechanical factors in allowing pathogenic agents to enter the pulmonary parenchyma

In these patients the local irritation and injury are supplied by an inability to get rid of the secretions In the presence of these irritations and injuries a virulent bacterium which is present as a part of an acute respiratory infection at the time of operation and injury often can originate pneumonia

A pneumococcal infection in a particular instance depends on the individual susceptibility to the pneumococci with which the patient comes in contact, provided the pneumococci possess sufficient virulence to produce disease.

The pneumococcus with its type specific polysaccharide capsule when introduced into the body of the host is capable of stimulating defensive mechanisms The immune substances include agglutinins, precipitins, opsonins and protective antibodies. Antibodies to pneumococci can be demonstrated in a large percentage of human beings It is assumed that the antibodies thus found in normal persons are the result of previous exposure to pneumococci, that is, of latent or manifest infection Normal carriers probably represent those who respond well to pneumococcus antigens and are, therefore, highly resistant to infection

The carrier state and the dosage and virulence of organisms received by the host are important factors in the production of pneumonia Equally important factors include the lowering of resistance of the individual by exposure, chronic disease, inanition and alcoholism Depression of protective mechanisms of the mucous membranes of the upper portion of the respiratory tract by viral and other infections is important

Pneumococcal Lobar Pneumonia The pneumococci are of the tribe Streptococceae and family Lactobacteriaceae They are gram-positive, frequently of lancet shape, usually arranged in pairs or short chains, and possess an easily demonstrable capsule

Of some 75 types of pneumococci, the 32 types commonly described as causative agents of pneumonia vary considerably in distribution Types I, II, III, V, VII, VIII and XIV are the most frequent in pneumonia Types I, II, and V usually are associated only with lobar pneumonia and are present in carriers only when the carriers have been in close contact with patients ill with lobar pneumonia In a series of 13,160 cases of pneumococcal pneumonia as recorded by Rosi, the types of pneumococci in order of prevalence were I, II, III and VII Pneumococci associated with healthy carriers are usually type III, and are present in one fourth to one half of healthy persons The consensus is that type III pneumococci are capable of causing pneumonia only in those who are debilitated or aged Type VI rarely provokes infection

PATHOLOGY The progress of the pneumonic process has been divided into three stages (1) engorgement, (2) red hepatization, and (3) gray hepatization The initial

before the whole lobe is involved It is thus revealed how it is possible to have engorgement, red hepatization and gray hepatization present in the same pneumonic lobe of the

lung Resolution occurs as the affected tissue becomes soft and friable. As the pneumonic process resolves, only a small part of the exudate is expectorated; the major portion is autolyzed by enzymes supplied by the degenerating leukocytes and macrophages and is resorbed

The incubation period ranges from a few hours to 1 or 2 days.

SYMPTOMS The onset of lobar pneumonia is characterized by a chill, fever, stitch in the side, nausea and vomiting The chill is often prolonged and is followed by a headache and generalized body aches. The temperature rises rapidly to 104 to 105 F (40 to 40 5 C) Very soon there is a short unproductive cough The cough is restrained because it enhances the pain. The pain is sharp and stabbing, and its presence seems to cut the cough short In rare instances the pain is absent. The face is red and the cheeks are flushed, often the cheek on the affected side is more flushed than the opposite cheek. The expectoration at first is scanty; it becomes blood streaked and then brownish, yellow or red in appearance The expectoration increases as the engorgement of the lung and the cyanosis increase.

The degree of cyanosis is somewhat of an index of the severity and extent of the pneumonic process Dyspnea and hyperpnea compensate only in part for the cyanosis, which is due to anoxemia dependent on alveolar edema and exudate which make impossible a free exchange of oxygen and carbon dioxide.

The pulse rate is increased, usually in proportion to the increase in temperature Circulatory failure, if it occurs, is not primarily myocardial in origin, but is more nearly related to circulatory collapse of the vascular capillary bed A sudden decrease in the blood pressure observed during the course of pneumonia is related to the tachycardia, prostration and dyspnea This evidence of circulatory strain in pneumonia is likely to occur more frequently in the obese, the alcoholics and the aged

A pneumonic crisis may occur within one day after onset or it may be delayed for two weeks or more The crisis is uncommon before the third day and rare after the twelfth A precritical rise, of a degree or two, of fever may occur Then within a period of from 5 to 12 hours the temperature returns to normal (often a fall of 6 to 8 F). After the crisis, the temperature is often subnormal, sweating is abundant and the patient falls asleep for several hours

There are all gradations of severity of lobar pneumonia In fulminating pneumonia there are prostration, shocklike reaction, and often pulmonary edema (wet pneumonia) These patients may die within a few hours from circulatory collapse In contrast, there are those who have fever of brief duration with crisis within 24 hours (abortive pneumonia) Ambulatory cases occur in which the course is mild and in which the lesion is detected on roentgenologic inspection only. Central pneumonia with location of the lesion near the hilus of the lung will often give no signs on physical examination However, within a few days physical signs will appear The involvement of one or more lobes on each side of the thorax has been referred to as double pneumonia, in which the prognosis is less favorable than with involvement of a single lobe In a massive pneumonia the bronchi of the involved region are often filled with exudate, and the physical findings may simulate pleural effusion In migratory pneumonia the process extends through the lobes of one or both lungs. In lethal instances of the disease in which there was little or no evidence of involvement of neighboring lobes detectable prior to death, necropsy frequently reveals such extension.

EXAMINATION. On examination the face, neck and hands are hyperemic or cyanosed. Dyspnea is present, and there is often a herpes labialis and a flushed cheek on the side of the lesion The respirations are increased at intervals to several times their normal rate. After consolidation has occurred, unless the bronchi are filled with thick secretion or fibrinous exudate, or unless pleural effusion is present, the vocal fremitus over the affected portion of the lung is increased and a friction

fremitus also may be felt If the consolidation is deep-seated, the resonance may be impaired or no changes can be elicited on percussion. The vocal fremitus, if the larger bronchi are not plugged, is increased

In the early stages the breath sounds are often enfeebled and may be suppressed. When the breath sounds are present at the end of inspiration, crepitant rales may be heard As engorgement advances into consolidation, the breath sounds become bronchovesicular and then bronchial in type.

The occurrence of persistent crepitant rales in the presence of systemic reaction, cyanosis and dyspnea—any one of which alone is significant—together is almost diagnostic of pneumonia A limitation of expansion on the affected side and pleural friction rubs are often present Impairment of resonance appears or increases in intensity with consolidation If the region of consolidation is small, its detection and delineation may best be facilitated by the increased intensity of tactile fremitus The demonstration of increased tactile fremitus depends on the extent of the involved space at the periphery and the experience and tactile sense of the examiner. If a bronchus becomes plugged by secretions, the atelectasis and absence of breath sounds with some impairment of resonance may be difficult to interpret until sudden clearing of secretions after cough or a change in position is made.

Sputum and blood for cultures should be obtained before chemotherapy is started The determination of the presence or absence of invasion of the blood stream is valuable in every case Streptococci or staphylococci or other organisms may prove to be the etiologic agent and their recognition is more important for therapeutic application than the type of pneumococci The presence of such organisms as Friedländer's bacillus or *Hemophilus influenzae* may be suspected from Gram's stains The susceptibility of the invading organisms to the various chemotherapeutic drugs as well as to the antibiotic agents has made the determination of these susceptibilities a standard procedure for the proper therapeutic results

Leukocytosis is the rule in pneumonia The usual counts vary from 15,000 to 25,000 per cubic millimeter of blood Increased leukocytosis may be present with complications such as empyema or pulmonary abscess. Reduction of leukocytes occurring with extension or complications, or at any time during the course of the disease, indicates an undesirable response and a low resistance to the disease.

Diagnosis Cyanosis, hyperpnea, dyspnea, fever and chills occurring in a previously well individual and attended by physical and roentgenologic evidence of pulmonary consolidation are distinctive of lobar pneumonia. In the presence of an acute exanthem, meningitis, or other severe systemic disease lobar pneumonia is not diagnosed until evidence of localization becomes apparent. Such localization as well as the extent of the pneumonia is more precisely located by means of roentgenologic examination

The early involvement of the pleura in the lower portion of the right lung field may cause referred abdominal pain This pain may simulate the pain of cholecystitis or appendicitis, so that time may be required in order to make the correct diagnosis

The organism producing the lobar pneumonia is determined by bacteriologic methods

In regard to the prognosis in pneumococcal pneumonia in recent years, two groups of patients who had this disease were studied by de Beradinis and de Andino. The first group of 75 patients was admitted during the period of 1937 to 1940. The second group consisted of 91 patients admitted during the period of 1946 to 1949 Comparison of the two groups showed that there was no decrease in the rate of admission of patients with pneumococcal pneumonia. In the years 1946 to 1949 there was an increase in incidence of the disease in higher age groups, with an increase in mean age from 39 9 years to 46 6 years There was also an increase in the occurrence of pneumococci of type IV and above with a corresponding fall in lower numbered types, especially type I Physical observations of lobar con-

solidation were made in 63 patients of the first group as compared with 35 in the second group. The percentage of septic complications fell from 16 to 7.7 per cent, probably as the result of antibiotic therapy. The over-all mortality rate fell from 21.3 to 6.59 per cent The majority of the patients who died had the complicating features of chronic degenerative disease, which influenced the mortality rate unfavorably in patients aged more than 40 years.

COMPLICATIONS. Empyema and pulmonary abscess are the commonest complications Empyema is suspected if there are (1) a lysis instead of a crisis of the fever, (2) recrudescence of fever, (3) a continuance of the increased leukocytosis, (4) sweats and a progressive inanition, and (5) the physical or roentgenologic evidence of free or encapsulated pleural effusion.

Delayed resolution, bronchiectasis, pulmonary fibrosis, pericarditis, meningitis, endocarditis, hepatitis, parotitis and purulent arthritis are of rare occurrence when sulfonamide or antibiotic therapy is employed

Bronchopneumonia. Bronchopneumonia is a diffuse process not often caused by the pneumococci. It is not lobar in distribution. A bronchial pneumonia differs from the so-called atypical pneumonias by the fact that etiology can be determined The disease most frequently is caused by beta-hemolytic streptococci Other causative organisms are *Hemophilus influenzae*, *Staphylococcus aureus*, gram-negative micrococci, and *Streptococcus viridans* Bronchopneumonia in adults is usually secondary to an acute infection of the upper part of the respiratory tract, influenza, measles or chronic disease It tends to be most frequent in early and late life.

SYMPTOMS Since bronchopneumonia is almost always secondary to a preceding illness, the symptoms are merged with those of that illness. The initial symptoms of bronchopneumonia are fever, cough and dyspnea. Rusty sputum is less frequent than in lobar pneumonia There may be a chill or a chilly sensation Pain develops immediately The fever is of the irregular, daily, fluctuating type. Prostration and signs of anoxemia vary considerably and while they tend to be less in bronchopneumonia than in lobar pneumonia, nevertheless a marked cyanosis may develop which is indicative of a severe process The symptoms of the disease may fail to have a respiratory localization, and thus there may be no respiratory symptoms Whether or not there are respiratory localization and symptoms, the fever tends to terminate by lysis. The duration of the disease is exceedingly variable and all symptoms may merge into those of a complication Complications are less frequent in bronchopneumonia, however, than in lobar pneumonia

The presence of acute respiratory symptoms and fever in a patient who has had influenza, measles or any respiratory infection which has reached epidemic proportions is accepted as pneumonia bronchial in origin until proved not to be of such origin

EXAMINATION. The physical examination reveals findings varying from those present in acute bronchitis to those of lobar pneumonia At times bronchopneumonia may involve almost an entire lobe of a lung. The presence of several localized re-

[illegible]

sounds.

DIAGNOSIS. A history of previous respiratory infection, physical signs and roentgenologic evidence in the thorax are conclusive

When bronchopneumonia occurs secondary to chronic disease, particularly in the advanced decades of life, high mortality rates are expected Following epidemics of measles, respiratory infection and influenza, a high mortality rate is the rule Increasing age, marked extent of pulmonary involvement, bacteremia, alcoholism, inanition and debilitating disease are all factors making for grave prognosis

Postoperative Pneumonia. This disease is bronchopneumonia occurring soon after a surgical operation. The predisposing causes of postoperative pneumonia (bronchopneumonia) are listed by Whipple as follows: (1) inflammations in the upper part of the respiratory tract present at the time of surgical operation; (2) vasomotor changes causing a congestion of the pulmonary vessels; (3) factors, during and after the operation, which inhibit the normal thoracic and abdominal respiratory movements and favor atelectasis and hypostasis in the lung; (4) local or general infections elsewhere than in the respiratory tract; (5) a lowered natural or acquired immunity to organisms which can incite pneumonia, and (6) increase in the virulence of the inciting organisms, for instance the presence of a virulent strain of streptococci causing endemic sore throats.

Postoperative pneumonia often begins as atelectasis with pneumonia developing in the collapsed portion of lung. The symptoms are those of bronchopneumonia. The onset of symptoms may be as early as the second postoperative day or delayed until the patient is out of bed The physical findings are likewise those of bronchopneumonia

The bedside roentgenologic examination is used as guesswork for diagnosis until the patient is able to be moved for physical examination and the regular roentgenologic examination

Post-traumatic Pneumonia. Thoracic injuries, especially fractured ribs which cause interference with respiration, are frequently associated with pneumonia. Interference with respiration appears to be the most important single factor in the occurrence and localization of pneumonia or atelectasis in post-traumatic as well as postoperative patients Interference with respiration also accounts for an occasional pneumonia after severe head injuries.

The etiologic agent in post-traumatic pneumonia is often a pneumococcus A rib fracture in an elderly person followed by infection with pneumococcus type III may have a serious prognosis Streptococci, staphylococci or other organisms are often the causative microorganisms and they too cause a serious pneumonia in a patient of any age

The symptoms are often obscured by those of the original injury The expectoration of blood often indicates a pulmonary hemorrhage A fever and leukocytosis associated with respiratory distress and hemoptysis are significant manifestations.

Following trauma, intrapulmonary hemorrhage may be the cause of physical signs like those associated with bronchopneumonia The physical signs after trauma are usually scattered with only at times those of consolidation of a lobe.

A presumptive diagnosis can be made if there are no evidences of intrapulmonary hemorrhage on roentgenologic examination

Prognosis is variable, depending on the resistance of the host in relation to age, chronic disease, alcoholism and the virulence of the invading organism

Pneumonia Due to Unusual Bacterial Agents. Infrequent agents causing pneumonia include bacilli such as *Hemophilus influenzae, Hemophilus pertussis, Bacillus pyocyaneus* (*Pseudomonas aeruginosa*), *Bacillus anthracis* and *Pasteurella pestis*, cocci, such as *Gaffkya tetragena*, meningococci and *Neisseria catarrhalis.* Pneumonia may also be associated with brucellosis, typhoid fever, diphtheria and rickettsial diseases

Acute Pneumonitis. The term acute pneumonitis is used by Adamson (in Myers and McKinlay) to indicate acute inflammation in the lung that is not only endobronchial but involves the parenchyma as well. The parenchymal involvement in acute pneumonitis is not sufficient to produce signs or symptoms of pneumonia The term thus includes many separate etiologic entities; yet if the definition of the term, as it is given by these authors, is adhered to, the underlying pathologic condition is definite and precise.

Adamson has arranged a convenient classification of pneumonitis which is essentially as follows. (1) common cold pneumonitis, (2) influenzal pneumonitis, (3) obstructive pneumonitis, (4) *exacerbation pneumonitis.*

1 **Common Cold Pneumonitis.** Gross pulmonary infiltration is found on roentgenologic examination of the thorax in many patients who have insignificant symptoms Often there is a history of a common cold or slight infection in the upper part of the respiratory tract A follow-up on these patients shows complete resolution in the course of a few weeks

Physical signs are usually absent

2 **Influenzal Pneumonitis.** The pneumonitis following influenza is essentially inflammatory, and that following infection of the upper part of the respiratory tract is *commonly obstructive In most instances of influenza the respiratory symptoms* commence after the first day after the onset, whereas in infections of the upper part of the respiratory tract the inception is with respiratory symptoms

Influenza is characterized by the sudden onset of headache, muscle pains, anorexia, chilliness, weakness, depression and general malaise If there is a localization of the discomfort, it is the backache and aching legs There may be signs or symptoms of respiratory inflammation varying from pharyngitis to pneumonitis or in some a definitely manifested pneumonia

There is a widespread bronchitis accompanied by retrosternal pain, and a *burning*, dry, *harassing* cough *with* scanty *sputum There may be coarse rhonchi* diffusely spread throughout both lungs Crepitations after coughing are commonly found about the bases which indicate definite parenchymal infiltration

On roentgenologic examination of the thorax there is a peribronchial infiltration which spreads out into the parenchyma from one or both roots The commonest site is in the medial half of the base, the cardiophrenic angle being frequently involved The extension may be into the middle third and not infrequently into the upper lobe In most cases the involvement is unilateral, but both lower lobes may be involved at the same time or in sequence Migration from place to place is common

Characteristically, influenza does not produce leukocytosis, and if the total leukocyte count is more than 10,000 per cubic millimeter, the pulmonary infection is due to or complicated by some pyogenic organism The common occurrence of *a relative bradycardia in influenza is of value in the recognition of influenzal* pneumonitis.

3 **Obstructive Pneumonitis ("Infection Atelectasis").** An obstructive pneumonitis may arise when there is an abnormal respiratory secretion It is characterized by sudden onset of pleural pain in the axillary line associated with shortness of breath Constitutional signs are mild or absent The physical and roentgenologic signs are those of pulmonary collapse, elevation of the diaphragm or displacement of the mediastinum

This condition requires treatment primarily directed to relief of obstruction

4. **Exacerbation Pneumonitis.** Pulmonary tissue damaged by previous inflammation may have as a consequence *an impairment of natural drainage* Reduced natural drainage is conducive to accumulation and stagnation of secretion and retention of infected material As the result of poor drainage local inflammation occurs which is a pneumonitis A variety of clinical effects may be produced, depending on the relative participation of the two factors, obstruction and inflammation, and the extent of the process

There is a history of colds, cough and purulent expectoration In a few cases there is the history of attacks with pain and fever. In the intervals between attacks the patients are free from symptoms, or chronic cough may persist The attacks are always *localized* and repeated in the same side

The physical signs and roentgenologic findings during any such attack are similar in a general way to those of any other form of pneumonitis

There may be signs of chronic infection enough to suggest chronicity. Such signs are clubbing of fingers, thoracic asymmetry, reduced movements, dullness or coarse rales which do not clear after coughing

Roentgenologic observations may suggest chronic rather than acute changes.

Pulmonary Abscesses. In a patient in whom the presence of a pulmonary abscess is suspected, the history of a surgical operation, particularly on the mouth, nose or throat, or of a recent attack of pneumonia is significant. Pulmonary abscesses may follow surgical procedures which are prone to give pulmonary infarcts, such as operations on the pelvis and hernial repairs They may occur during the course of a septicemia such as endocarditis or furunculosis. History of an attack of choking while swallowing food, or an attack of cough following aspiration of some other object, is significant from the standpoint of abscess due to foreign body In some patients who have pulmonary abscesses there is no history of pre-existing conditions such as those just mentioned. This is particularly true of pulmonary abscesses in children following aspiration into an air passage of a foreign body which supposedly was coughed up

The pyogenic abscess is usually caused by the pneumococcus, *Staphylococcus aureus*, and the hemolytic streptococcus Anaerobic organisms which normally inhabit the

can produce lung abscesses

A pulmonary abscess may arise from an infected embolus causing infarction, and secondarily abscess formation In other instances lodging of a sterile embolus produces infarction, organisms are aspirated from the mouth, nose and throat and infect the infarcted region in the lung, and thus an abscess is formed In some instances both processes are present, namely, an infected embolus and the aspiration of infected material from the nose, throat and trachea

The prime factor which favors the chances of abscess formation after operations on the nose, mouth or throat is the use of general anesthesia for the operation. The general anesthesia abolishes the cough reflex and thus permits aspiration of infected material from the upper air passages

Pulmonary abscesses often result from the aspiration of foreign bodies into a bronchus Abscesses due to aspirated foreign bodies are more frequently found in the lower lobes, especially the right Once the foreign body is lodged in the bronchus, it ulcerates through the wall of the bronchus into the pulmonary tissue, and abscess formation ensues The object for abscess formation may be of intrapulmonary origin, for instance, Vinson called attention to calcifications produced by the first infection type of tuberculosis in hilar lymph nodes which ulcerated into bronchi and were aspirated into their ramifications, causing abscess Other causes of pulmonary abscess are obstruction of bronchi by tumors and pneumonia.

SYMPTOMS A chill followed by fever similar to that observed in pneumonia may be the first manifestation of pulmonary abscess In the beginning of the disease cough and expectoration are slight or absent As the condition progresses, the cough begins and increases in severity Pleural pain and the sudden expectoration of a quantity of sputum with a foul odor are common manifestations. Abscesses which follow operations and aspirations from the mouth and throat usually are of sudden and severe onset There are profuse sweating and prostration Pulmonary abscess does occur with less severe initial symptoms, being manifested only by a general aching of the body and malaise Spitting of blood, varying in amount from streaks in the sputum to fatal hemorrhage, occasionally occurs even in those who have mild symptoms The symptoms of multiple abscesses due to septic emboli often are masked by the symptoms of the main disease. During the course of septicemia or pyemia the first symptoms of a pulmonary abscess or abscesses may be

thoracic pain, cough and expectoration. No one symptom or combination of symptoms is pathognomonic of pulmonary abscess since all may be caused by other diseases.

EXAMINATION Inspection often reveals clubbing of the fingers and toes, sometimes within a few weeks after onset of the abscess. Hypertrophic pulmonary osteoarthropathy develops in some instances. Limited movement of the thoracic wall on respiration often occurs on the affected side, and the phrenic wave sign is decreased or absent If the abscess has an acute severe onset the patient appears seriously ill

If the abscess is small, no abnormal signs are elicited by palpation If the abscess is large, with extensive inflammation of the adjacent pulmonary tissue, tactile fremitus is increased except in the presence of pleural exudates, when it is diminished or absent The reflex protective mechanism consists of a rigidity of thoracic muscles which can be elicited and palpated by tapping on the chest over the affected area with the end of the stiffened fingers.

The percussion note is normal if the abscess is small, but when it is large and near the surface, a dull to a flat sound is elicited Over large cavities near the surface of the lung a tympanitic sound may be heard when the cavity or cavities are empty

On auscultation the breath sounds are normal if the region of disease is small, but as it becomes larger, bronchial breathing appears. If large cavities are near the surface and are partially or totally empty, amphoric breath sounds may be heard Changes in the spoken and whispered voice sounds depend on the extent and situation of the disease Voice sounds are normal when normal lung tissue is superimposed over the abscess but are heard distinctly over the areas where bronchial breathing is elicited, and if large empty cavities exist, pectoriloquy may be present Rales are usually heard when the region of disease is large and near the surface These may be consonating if cavities are only partially filled

DIAGNOSIS The foregoing symptoms and physical signs may be definite enough for the purpose of diagnosis, when interpreted and correlated with the history.

Roentgenologic examinations often determine the location and extent of gross disease, although some abscesses are not located by this means. Large abscess cavities, when completely filled with pus, present no fluid level; their outlines may not be seen, so that their presence is not detected on roentgenologic examination. If evacuation of the abscess cavity or cavities, as by postural drainage, can be accomplished, then iodized oil can enter, after which the roentgenogram affords good evidence as to size and location of cavities Endoscopic inspection of bronchi should always be made if there is doubt as to either the presence or the etiology of an abscess

Pulmonary abscesses may occur in tularemia, brucellosis and amebiasis. Inasmuch as tuberculosis may coexist, a search is made for tubercle bacilli and if there is doubt, guinea pig inoculation is performed

A single abscess may heal spontaneously in 1 of every 4 cases In the remaining 3 cases the prognosis is guarded The poor prognosis in many is due to conservatism and the lack of surgical skill Spontaneous recovery rarely occurs if the disease is allowed to persist more than a few weeks Surgical treatment as soon as the diagnosis is made markedly improves the prognosis

Pertussis (Whooping Cough) The genus *Hemophilus pertussis* (whooping cough bacilli), type *Hemophilus influenzae*, belongs to the family of Parvobacteriaceae

Strains of *Hemophilus pertussis* on primary isolation constitute a single antigenic type. They are gram-negative. The organisms can be identified serologically by the agglutination test

The distribution of pertussis is cosmopolitan The disease is endem[illegible] ies

occur at intervals of two to four years in the more thickly populated areas, beginning in winter, or spring, and lasting throughout the summer months In the South the disease spreads during April and May, in the North January and February are the peak months. Pertussis is distinctly a disease of early life except in some women, particularly in the older age groups Infants less than 6 months of age are especially susceptible, and among them the disease has a higher mortality. The communicability rate is high, particularly in family exposures in which it is from 75 to 90 per cent.

IMMUNITY. Although an attack usually confers lasting immunity, second attacks do occur.

Active immunity against the disease can be induced by the injection of an antigenic strain of the organisms Passive protection may be given to an infant by the injection of convalescent serum, hyperimmune human serum, or immune rabbit serum. It is not generally transferred transplacentally but can be produced in this manner by actively immunizing the pregnant mother during the third trimester of pregnancy.

A profuse catarrhal inflammation of the epithelium in the larger air passages is always present. Purulent exudate and an excess of mucus accumulate in the lumina of the smaller bronchi and bronchioles. Peribronchiolitis is common, extending from the hilus outward along the blood vessels which accompany the bronchi to the middle or outer portions of the lungs.

The tracheobronchial lymph nodes are usually enlarged during the active and early convalescent stages of the disease and produce the characteristic hilar lesion commonly observed on roentgenologic examination

In addition to the pulmonary lesion produced by *Hemophilus pertussis,* secondary invading organisms may cause purulent bronchitis, and even lobar pneumonia Bronchiectasis may develop early in the course of the disease but it is commoner as a sequela Emphysema is almost always present, blebs on the surface of the lung being observed in practically all cases in which death ensues Changes in the brain are described as circulatory, degenerative, and inflammatory Meningitis and encephalitis result from inflammation

SYMPTOMS The incubation period is from 10 to 14 days. The clinical course consists of three stages the catarrhal, paroxysmal, and convalescent; each lasting approximately 2 weeks Spasmodic coughing may occur for several weeks or months longer

The first symptom commencing with the catarrhal stage is a mild nocturnal cough, which soon becomes diurnal The cough develops as that of a bad cold, but the appetite fails as the cough increases in severity, and there is a suffusion of the conjunctivae with edema of the lower eyelids.

Toward the end of the second week the paroxysmal stage commences The cough becomes a series of explosive efforts of violent expiratory coughs during which inspiration is impossible Finally inhalation is performed through a markedly spastic larynx, and there is a rather loud, high-pitched inspiratory noise called the whoop During the period preparatory to the whoop and soon thereafter the veins of the neck and forehead are prominent, the face becomes congested and cyanotic, and mental confusion results In infants the characteristic whoop may not occur, but choking, cyanotic attacks are common

The convalescent stage commences after a month of coughing, and the paroxysms diminish in frequency and severity The appetite improves If a cold develops during convalescence, all the symptoms may reappear and continue for several weeks more if a superimposed bronchitis remains active

Pertussis may be extremely mild and may last only a few days without definite paroxysms, whoop, or vomiting

At any time during the course of the disease complications may supervene and the symptoms and physical findings are accordingly changed

Bronchopneumonia is a serious complication Atelectasis, bronchiectasis, pulmonary fibrosis, and emphysema, either vesicular or interstitial, develop in many instances when the disease is severe Pneumothorax and empyema may occur

Subcutaneous emphysema occurs when air from ruptured surface blebs escapes by way of the mediastinum into the tissues of the neck and thorax. In whooping cough, in contrast to spontaneous pneumothorax, subcutaneous edema is a serious complication and implies a fatal outcome.

Convulsions are most commonly limited to infants Encephalitis, epilepsy, mental retardation, visual defects, temporary paresis and hemorrhages of the brain are described

Secondary mechanical effects attributed to the strain of coughing are conjunctival hemorrhages, epistaxis, ulcer of the lingual frenum, intussusception, hernia and rectal prolapse Often as the result of coughing in adolescents there is soreness of the muscles of the lower part of the thorax and particularly of the upper part of the abdomen

EXAMINATION. The findings on examination by physical means depend on the stage of the disease and the presence or absence of complications when the patient is examined During the course of mild to moderate degrees of severity of the disease there may be very few or no significant physical findings. In the severe instances of the infection there are various sorts of rales throughout both lungs The presence of crepitant rales in any part of the lung often signifies the onset of a bronchial pneumonia in the region where the rales are present

A *progressive increase in the total leukocyte count occurs* during the late catarrhal or early paroxysmal stage These cells may increase to 15,000 to 45,000 per cubic millimeter of blood as the result of lymphocytosis

DIAGNOSIS A history of definite exposure is of much diagnostic value A modified type of the disease may be expected when vaccination fails to protect completely

Hemophilus pertussis may be isolated by cultures from the respiratory tract. During the catarrhal period positive cultures may be expected in from 70 to 90 per cent of the cases.

The diseases which may produce symptoms simulating those of pertussis are infection of the adenoids or nasal sinuses, allergic reactions, and infection of the trachea with *Hemophilus influenzae*. Parapertussis resembles mild pertussis and can be differentiated only by culture

The mortality rate is about 25 per cent during the first year of life and 10 per cent during the second year The disease is seldom fatal after the fifth year.

Hemophilus Parapertussis (Bacillus Parapertussis). *Hemophilus parapertussis* is a short, ovoid, gram-negative, nonmotile bacillus which in many respects resembles *Hemophilus pertussis* It is the cause of parapertussis, a disease which resembles mild pertussis, from which it can be distinguished only by bacteriologic methods

The incubation period of the disease in man is from 6 to 15 days The onset is similar to that of whooping cough, but may be more abrupt The cough is less severe than that of whooping cough, but is spasmodic, and is sometimes followed by a whoop Vomiting is less frequent than in whooping cough. The entire course of illness is from 1 to 3 weeks The disease often resembles tracheitis

It is not known whether one attack of parapertussis confers lasting protection An attack of parapertussis *does not confer immunity against pertussis*, nor does an attack of pertussis confer protection against parapertussis.

Pulmonary Tuberculosis. *Primary Phase.* In the majority of those who have pulmonary tuberculosis there is a known exposure to the disease. In children often the exposure has been prolonged. Prolonged exposure to contagious tuberculosis is not necessary for the acquisition of a sufficient number of tubercle bacilli to become infected, for an exposure of seconds of time under proper conditions may be adequate for the transfer of large numbers of organisms

Tuberculous infections are divided into the primary phase, or the first infection, and the secondary or reinfection tuberculosis.

The National Tuberculosis Association defines the primary phase of a tuberculous infection as the pathologic processes which follow directly and uninterruptedly the first implantation of tubercle bacilli.

In the first infection by tubercle bacilli the organisms gain entrance through the nose, mouth, eyes, abrasion of the skin or through the genital tract. The bacilli are phagocytosed by neutrophilic cells After the bacilli are in these cells, they may be inactivated or deposited in the tissues and are thus focalized These neutrophilic cells containing tubercle bacilli may enter the blood and may be carried about in the blood stream to lodge in those parts of the body most richly supplied with fine capillaries. Thus lesions may be originated as focal disease in the lungs, bones, joints, lymph nodes and meninges

The first infection of tuberculosis usually is caused by inhalation of tubercle bacilli. The primary infection focus consists of a small tuberculous pneumonia often situated in the lower parts of the upper lobes, or in the upper parts of the lower lobes, near the pleura The center of the focus undergoes caseation rapidly (parenchymal focus) As caseation proceeds, tubercle bacilli are liberated and carried through the lymph channels to the regional bronchopulmonary lymph nodes

The primary complex heals promptly. However, in children exposed to prolonged infection it may not heal A failure to heal may result in a parenchymal lesion which may ulcerate into a bronchus and permit of bacillary dissemination through the bronchial system The primary hilar lymph-node foci may ulcerate into an adjacent bronchus, and cause a fatal tuberculous bronchopneumonia.

SYMPTOMS In the first infection type of tuberculosis, the symptoms simulate a bad cold or influenza The febrile reactions of this type of tuberculosis are of short duration, usually lasting not longer than 10 days or 2 weeks The temperature ranges between 99 and 101 F (37 2 and 38 3 C)

It is only when the primary infection fails to heal, and forms a parenchymal pneumonia which ulcerates into a bronchus, or when the hilar lymph nodes ulcerate into a bronchus, that the primary infection causes a serious disease such as a bronchopneumonia These primary bronchopneumonias may cause death The serious manifestations of a primary infection may occur at any age and are not limited to children.

EXAMINATION In the usual instance of first infection tuberculosis the physical examination is of no value in the detection of the tuberculous process in the lungs of children or adults

It is usually stated that when healing of the primary complex occurs, two signs are left The first sign comprises the lymph-node foci which partially or entirely heal and become calcified Even though calcification has occurred in the lymph nodes, viable tubercle bacilli may remain The second and the most definite sign left to indicate the presence of the primary complex is the fact that the body has become allergic to tubercle bacilli or their metabolic products, which can be demonstrated by positive tuberculin reactions

Positive findings on roentgenologic examination are present in but a few of those who are affected with a first infection type of tuberculosis.

Several years after the first infection type of tuberculosis, there may appear on the roentgenograms sharply outlined shadows in the pulmonary parenchyma or the hilar region which represent dense deposits of fibrous tissue, calcium or bone as the result of first infection tuberculosis This is a Ghon lesion or complex.

Tuberculosis as the cause of calcification in the lungs and hilar region is responsible in only one-half the instances in which calcifications are visualized by roentgenologic examinations (see Calcifications of Lungs, page 617).

Reinfection Phase. Following the advent of the primary infection with pulmonary tuberculosis a latent period intervenes. This latent period may last indefinitely if reinfection does not occur The latent period is the time supervening between the primary infection and the reinfection and the development of symptoms from the reinfection

The sources from which the reinfection is derived are always listed as exogenous and endogenous reinfections The exogenous source is from anywhere that live virulent tubercle bacilli may be obtained.

There are four sources of *endogenous* reinfection: (1) a primary pulmonary focus of the lung may break down and discharge bacilli into other parts of the lungs; (2) a caseated primary regional lymph-node focus may rupture into a bronchus, causing a tuberculous aspiration bronchopneumonia; (3) an active primary regional lymph-node focus, situated inside or outside of the lung, may send tubercle bacilli to the lung or other parts of the body by way of the lymphatics and the blood stream, (4) small apical foci which have developed as a result of early hematogenous dissemination frequently become progressive, ulcerate, and discharge bacilli into the bronchi.

Three forms of tuberculosis are discussed here

1 ***Miliary Tuberculosis.*** Miliary tuberculosis is caused by the discharge of the contents of a tuberculous lesion into either the blood or the lymph streams Hematogenous dissemination may occur during the active phase of the primary infection type of tuberculosis or as a terminal miliary spread in the reinfection type of the disease It is commoner in those who have not had symptoms of tuberculosis than in those who have had symptoms.

Many of the tubercle bacilli that reach the blood stream are filtered out by the lungs, kidneys, peritoneum, bones and the central nervous system. However, in 4 cases of each 5 the main localization is in the lungs due to the extent of the capillary bed here

The symptoms commence with weakness, malaise and fever, which increase in severity. The temperature ranges from 101 to 104 F (38 3 to 40 C) The respiratory rate is normal at first but increases, and cyanosis of a marked degree develops in the late stage of the disease. Cough is slight in the beginning but becomes distressing as the fever and cyanosis develop The sputum is scant

On examination the patient appears seriously ill Results of examination of the thorax by physical means are negative Roentgenologic examination of the thorax usually is not helpful in the beginning of the disease Ophthalmoscopic examination may reveal the presence of tubercles in the retina

In the presence of a more continuous fever, a greater failure of health, a more rapid loss of weight, and a more severe weakness in a patient known to have tuberculosis, a presumptive diagnosis of miliary tuberculosis can be made In all others, signs of localization, usually in lungs, must be awaited. Tubercles may be found in the retinae and may be the first definite diagnostic sign. Often in severe fulminating instances of the disease the diagnosis is not made during life except in those known to have tuberculosis. In the late stage, in approximately one-half of those who have miliary tuberculosis, a large number of small shadows appear in the roentgenograms of the lungs, and may be the first definite diagnostic finding

2. ***Tuberculous. Pneumonia (Galloping Consumption).*** A tuberculous pneumonia may result from a lesion of the primary phase eroding into an air passage and discharging its contents into the lumen A discharge of the tubercle bacilli into the bronchi may originate from a chronic reinfection type of lesion and cause a pneumonia. Occasionally a small focus of either the primary phase or the reinfection type of the disease may rupture into a blood vessel so that he bacilli

are disseminated into that part of the lung which this vessel supplies. This may involve a part of a lobe, a whole lobe, or an entire lung. When large regions of pulmonary tissue are affected, the hypersensitiveness caused by the tuberculoprotein aids in a necrosis of the tissues and a rapid development of pulmonary cavities

SYMPTOMS The disease frequently occurs in those who seemingly have been in good health. At the onset the symptoms are those of lobar pneumonia or of bronchopneumonia In some instances the onset is sudden, commencing with chills, high fever and pain in the thorax.

The onset may be more slowly progressive, with cough, fever, aching of the body, anorexia and malaise These symptoms soon begin to be more severe There is a rapid loss of body weight and the cough is severe. Sputum appears, increases in amount, is yellowish or greenish and streaked with blood, often profuse hemorrhages occur

EXAMINATION The patient is seriously ill The cheeks are flushed and sunken and the eyeballs are soft and retracted. The respirations are increased, profuse sweating and chills are regularly observed

On examination of the lungs, palpation, percussion and auscultation reveal the findings of pneumonia In many instances the signs of cavitation appear at short intervals after the disease has begun Reports on examination of sputum are positive for large numbers of acid-fast bacilli which on culture and guinea pig inoculation prove to be tubercle bacilli

DIAGNOSIS The diagnosis is made by recovery of tubercle bacilli from the sputum The physical and the roentgenologic examinations reveal pneumonia.

In most cases of massive tuberculous pneumonia the prognosis is grave, as death usually ensues within a few weeks There is no specific treatment

3 ***Chronic Forms of Pulmonary Tuberculosis.*** In the chronic forms of tuberculosis the organisms may be either the human or the bovine type (rarely avian according to Feldman) Chronic ulcerative and progressive pulmonary tuberculosis is a reinfection type of the disease in adults and occasionally in children.

There is no good evidence that race and nationality predispose to the development of pulmonary tuberculosis The incidence of the disease in the Negro and the American Indian probably is due to poor sanitation which predisposes to contagion rather than reduced resistance The members of both races respond to tuberculosis control measures.

The development of pulmonary tuberculosis following whooping cough, measles, pneumonia, or pregnancy is probably coincidental to an environment full of the germs of tuberculosis The development of pulmonary or any form of tuberculosis in the diabetic patient is serious

Trauma does not cause tuberculosis The discovery of pulmonary tuberculosis in a recently injured individual is an accidental finding and has nothing to do with the injury

Chronic pulmonary tuberculosis frequently results from hematogenous spread of tubercle bacilli Insufficient numbers are released to cause a general miliary tuberculosis, consequently fewer bacilli are deposited in various places in the body, and the body is more able to cope with them The initial lesion, the tubercle, is a small lesion These smaller lesions extend into the air passages, particularly the smaller bronchial ramifications, after which sputum containing tubercle bacilli is expectorated, shadows on the roentgenograms appear, and other symptoms become evident

Chronic pulmonary tuberculosis may be produced by exogenous reinfections, by inhalation of tubercle bacilli, or by ingestion of the bacilli into the digestive tract,

from which they are taken up by the lacteals. They reach the blood stream and lodge in the lungs.

From either endogenous or exogenous reinfections bacilli may reach the larynx and pharynx by way of the trachea, may reach the digestive system through the esophagus, and may reach the urogenital organs, the nervous system and bones through the blood stream

Chronic pulmonary tuberculosis is most commonly situated in the upper lobes of the lungs but may appear anywhere in the lungs. There is a strong tendency for such lesions to undergo remissions and exacerbations, and at any time they may be permanently arrested or may continue to progress and cause damage beyond repair

SYMPTOMS A history of exposure to those who have open tuberculous lesions capable of discharging bacilli is obtained from less than one-half of the patients who have active pulmonary tuberculosis

The consensus is that the allergic reaction to the tuberculoprotein is responsible for the acute manifestations of tuberculosis. However, the greater part of the symptoms of pulmonary tuberculosis are due to a toxemia The toxemia is manifested by its effects on the sympathetic nervous system and endocrines, particularly adrenals and thyroid Pottenger enumerated the symptoms due to toxemias thus (1) malaise, (2) lack of endurance, (3) loss of strength, (4) nervous instability, (5) diminished digestive activity, (6) increased metabolic rate, (7) loss of weight, (8) increased pulse rate, (9) fever and (10) night sweats Any one, or any combination, of these symptoms may be present in tuberculosis. Every one of these symptoms may be present in a patient who does not have tuberculosis A patient may have advanced active tuberculosis and not have any of these symptoms

Malaise is so common a complaint in those who are well or sick that it has little or no diagnostic significance at any time If present, it is due to toxemia

A *lack of endurance* is not significant if it is detached from the past performance of the patient It is significant if the patient is unable to endure more than a small part of the day's work which has been performed in the past without exhaustion.

The *loss of strength* is a comparative estimation in regard to past performance without fatigue Patients may state that they are unable to do work, requiring the same strength, that they did easily in former years. In the young man or woman this may be significant In aging men and women who do not have pulmonary tuberculosis this is their most common complaint

Diminished digestive activity is often an early symptom in pulmonary tuberculosis It is accompanied by a loss of body weight. Pulmonary tuberculosis is one of the common causes of loss of weight. A loss of several pounds during a few weeks is always significant Indigestion often appears intermittently Digestive disturbances may be severe in one, and mild or even absent in another who has tuberculosis

The *pulse rate* in pulmonary tuberculosis, as in normal health, varies considerably Fever is attended by an increased pulse rate.

Fever is a significant symptom of early pulmonary tuberculosis. The presence of fever is determined by recording the temperature every 2 hours for a period of 4 or 5 days. Elevations of temperature do not always occur at the same time of day or night on successive days. The common opinion that the fever appears only during the afternoon is often correct If the temperature is taken by mouth, the thermometer should be held under the tongue for 10 and preferably 15 or 20 minutes To be of significance it must be 99 F (37.2 C) or more for men and 99.6 F (37.5 C) or more for women, and should not show wide variations from hour to hour. In those who have a wide range of fluctuation, the morning temperature may be as low as 97 F (36.1 C)

Temperature greater than 99 F may occur intermittently, for instance, elevated for a few days, then absent for a time. Three or 4 weeks of observation may be necessary in some instances to be certain fever is present. There is usually a slight elevation of temperature associated with the menstrual period or at the time of ovulation a week or two before the period. Slight elevations in temperature may occur after exercise

Night sweats are of frequent occurrence. These sweats occur after midnight while the patient is sleeping soundly.

Tuberculous patients may complain of *huskiness* or *hoarseness* of the voice without detectable changes in the larynx Huskiness of the voice occurs as a part of general weakness and may accompany any low-grade fevers from any cause.

Tuberculosis is one of the causes of *cough.* Acute and chronic respiratory infections, air contaminants, allergy, mitral stenosis and intrathoracic pressure are examples of some of the common causes of coughs Many tuberculous patients who have a cough attribute all the symptoms to it. They feel no pain or other sensation within the thorax but have an almost constant *tickling in the throat* This symptom is a reflex one. In early tuberculosis the cough may be nonproductive.

Thoracic pain is commonly present in those who have tuberculosis In the absence of pleural pain, which is manifested in association with inspiration, a person who has tuberculosis frequently complains of pains about the shoulders and in the thorax Pains of this distribution, however, are often complained of by those who do not have tuberculosis

The spitting of *blood-streaked sputum* may be the subject of complaint in tuberculosis as well as in many other conditions of the nose and throat Hemorrhages, varying in amount from 1 dram to the point of exsanguination and death, may occur. Death results from pulmonary hemorrhage in one third of tuberculous patients Contrary to former-day teaching that blood-streaked sputum often indicated pulmonary tuberculosis it is now known that hemorrhage from the lungs occurs much more frequently in nontuberculous conditions, such as bronchiectasis, than it does in pulmonary tuberculosis Patients are not fearful of small hemorrhages, for there are those who give histories of hemorrhage for months or a year or more before reporting for examination

A hemorrhage may be the first manifestation of a tuberculous lesion which

Sputum, if present in the early stages of tuberculosis, often is in small amounts, thin and clear, and resembling saliva As the disease advances, the sputum increases in amount, becomes thicker, and attains a yellow or green coloration

Frequent bad *colds* and *cough* which persist for weeks are manifestations of a failure in health There are many causes for such bad colds, but among these causes pulmonary tuberculosis is an important one

A preceding or a present attack of pleurisy is often the first clinical manifestation of tuberculosis

EXAMINATION On examination the patient often appears to be in good health, or there may be evidence of loss of body weight and flabbiness of the muscles. As the disease progresses, an extreme state of emaciation may develop. Often there is a detectable decrease in the expansion of the thoracic wall over the region of disease The excursion of the diaphragm is limited, hence the phrenic wave (Litten's sign) *is limited in range of excursion*

Often a patient who has pulmonary tuberculosis has a flushed condition of the cheeks The flushing may appear only at certain times of the day and is not synchronously present with fever The reddened cheeks may be unilateral or bilateral,

corresponding to the side of the lesion or lesions. The patient may complain of a hot sensation of the ear or the side of the face without the appearance of flushing. The burning and the flushing are due to dilatation of the blood vessels to the regions, produced reflexly by the stimuli passing upward over the vagus and peripherad over the fifth cranial nerve.

When the disease attains the moderately or far advanced stage, tactile fremitus is present. The percussion note is dull or flat over the involved portions. Auscultation reveals changes in breath sounds, varying from bronchovesicular to bronchial breathing. The whispered and spoken voice sounds are more audible over the tuberculous lesions than over the normal lung. Bronchophony may be elicited over sites of solidification, and pectoriloquy over the empty or partially filled cavities. Rales of the fine or moderately coarse variety are heard over the regions of disease which have reached the moderately or far advanced stage. Rales of a metallic or resonating quality are heard over cavities.

DIAGNOSIS OF PULMONARY TUBERCULOSIS. The following discussion is essentially an adaptation of material in *Diagnostic Standards and Classification of Tuberculosis* (1950), of the National Tuberculosis Association, and, in part, a quotation from that text. This material as adapted here is used by permission of the Association.

The diagnosis of tuberculosis includes a determination of the presence and situation of a tuberculous lesion and an evaluation of its pathologic characteristics; that is, whether the lesion is open or closed. Open lesions disseminate tubercle bacilli and therefore are dangerous or potentially dangerous to the patient and those with whom contact is made.

Because active open pulmonary tuberculosis often exists without symptoms or abnormal findings, both pulmonary tuberculosis with symptoms and pulmonary tuberculosis without symptoms are considered.

Pulmonary Tuberculosis Without Symptoms. The repeated roentgenologic examinations of apparently healthy contacts of known cases of tuberculosis disclose many asymptomatic but actually open and potentially dangerous lesions, particularly in adolescents. The mass roentgenologic examinations of apparently healthy groups in occupations or at ages in which tuberculosis mortality rates are relatively high have revealed lesions which may prove on further investigation and study to be minimal in extent but amenable to treatment.

Further study and observation of these minimal lesions consist of history, physical examination and serial roentgenologic examinations made at regular intervals of one to two months to determine the degree of instability of lesions. Sputum studies are made from time to time, temperature records are kept until it can be determined whether a lesion is active and in need of treatment. Reactors to tuberculin should be examined roentgenologically each six months to one year.

When applied to adolescents and adults, mass roentgenologic examination of the lungs has as its primary object the detection of active or potentially active tuberculosis. Mass tuberculin testing is commonly restricted to those of elementary school age or less, although in rural communities and other low-incidence areas it may be used to advantage among older age groups as a preliminary screening method.

Pulmonary Tuberculosis With Symptoms. Tuberculosis in its early stages seldom [illegible] atient to consult a physician. [illegible] there is constantly a history [illegible] chest pain, dyspnea, hoarseness, cough, and hemoptysis. The history of lassitude, loss of appetite, loss of weight, and slight elevation of temperature, and night sweats occurring in a young individual is particularly significant. A physical examination may reveal moist rales over a limited area of the upper third of one side of the chest. Occasionally the

abnormal signs are elicited over only a lower lobe. Such findings require a roentgenogram to be made of the chest; and, if there is sputum, it is examined for acid-fast bacilli. If negative on direct smear, specimens should be concentrated and, if necessary, culture or guinea pig inoculation is made If there is no sputum, gastric contents are obtained while the patient is fasting and are cultured or inoculated into guinea pigs The tuberculin test is given at the time of the first visit so that readings of the results may be made two or three days later. A negative reaction to a tuberculin test is strong evidence that the physical findings are not due to tuberculosis. A tuberculin reaction in itself should not be regarded as an indication of dangerous tuberculous infection, except in infants.

Obviously both the tuberculin test and the roentgenogram are of value in differential diagnosis of pulmonary disease. Occasionally repeated stereoscopic films and examinations in the lateral, oblique, and lordotic positions may be of definite value.

TUBERCULOUS COMPLICATIONS Three major complications of pulmonary tuberculosis are those in the larynx, the trachea and the bronchi. The larynx can be viewed readily. The trachea and bronchi require bronchoscopic examination, and sometimes even this will not lead to the diagnosis if the lesions are beyond the bronchoscopist's limited scope of vision. Tracheal or bronchial lesions may give no symptoms and yet produce positive sputum Lesions of the trachea rarely cause wheezing. The main clinical symptoms of bronchial disease are wheezing, severe coughing, and otherwise unexplained dyspnea, all of which are the direct result of reduction of the lumen of the bronchus Massive collapse of a segment of a lobe, of a lobe, or an entire lung sometimes results from this interference with aeration and drainage. The progress of this complication may seriously affect the management of a parenchymal pulmonary lesion

Involvement of the pleura is practically a constant finding in well-developed pulmonary tuberculosis Pleural effusions in young patients should be considered as of tuberculous origin unless proved otherwise A diagnostic tap for laboratory studies of the fluid is usually indicated Often at the time a patient complains of pain in the chest, immediate fluoroscopic or roentgenologic examination may not reveal evidence of effusion Repeating the examination after the pain has subsided will frequently result in the discovery of a pleural effusion

DIFFERENTIAL DIAGNOSIS OF PULMONARY TUBERCULOSIS The commoner conditions to be differentiated from pulmonary tuberculosis are the pneumonias, pulmonary abscess, low-grade bronchiolitis secondary to chronic sinusitis, bronchiectasis, neoplasms (especially bronchogenic carcinoma), various pulmonary fibroses (especially silicosis), sarcoidosis and fungous infections.

cavities and exudative lesions The symptoms are those of a prolonged influenza, and the diagnosis rests on the recovery of *Coccidioides immitis* from the sputum or pleural fluid Histoplasmosis is found chiefly in the Middle Western and Southeastern states, and it is not uncommon in these areas to see a number of small calcifications in roentgenograms of patients who have negative tuberculin and positive histoplasmin tests.

In sarcoidosis, patients often fail to react to the tuberculin test and have few if any symptoms in spite of roentgenograms showing hilar adenopathy and pulmonary lesions like those of far advanced tuberculosis, miliary tuberculosis or silicosis

Roentgenologic shadows are never pathognomonic, and when a person is in the age period in which cancer is most frequent, and specific evidence of tuberculosis or other disease has not been obtained, examination for malignant tumor should always be made.

SCREENING CLASSIFICATIONS USED IN MASS ROENTGENOLOGIC SURVEYS. During the years the public has become conscious of the ravages of tuberculosis and has done much through sanitary methods in the home and by demanding purer milk supplies to control this disease. Those in charge of mass roentgenography seem to think that this method has been successful in the finding of many who have pulmonary lesions requiring further study.

As the use of this technic increases, the need for uniform standards and classification of screening-film findings becomes apparent. The systematic terminology used by the National Tuberculosis Association which has proved to be practical and informative is presented here:

CLASSIFICATION OF PULMONARY TUBERCULOSIS *

Extent of Pulmonary Lesions. *Minimal.* Slight lesions without demonstrable excavation confined to a small part of one or both lungs. The total extent of the lesions, regardless of distribution, shall not exceed the equivalent of the volume of lung tissue which lies above the second chondrosternal junction and the spine of the fourth or body of the fifth thoracic vertebra on one side

Moderately Advanced. One or both lungs may be involved, but the total extent of the lesions shall not exceed the following limits.

Slight disseminated lesions which may extend through not more than the volume of one lung or the equivalent in both lungs.

Dense and confluent lesions which may extend through not more than the equivalent of one-third the volume of one lung.

Total diameter of cavities less than 4 cm

Far Advanced Lesions more extensive than moderately advanced

Extent of Pulmonary Lesions Following Therapy. In the case of temporary collapse, the extent of disease existing immediately before the collapse shall be continued in the classification until re-expansion permits reclassification

In the case of permanent collapse or pulmonary excision, the extent of disease in a lung existing immediately before excision or collapse shall be continued in this classification through life, except that such extension or new deposits of disease as appear any time postoperatively in this or the contralateral lung shall be additions to the preoperative classification. The form, site, and duration of the procedure shall be added in parenthesis to the classification of extent of disease.

In other cases the classification of extent will be changed as the change in the extent of the demonstrable lesion warrants Once the diagnosis of pulmonary tuberculosis has been established, however, the extent of the lesion cannot be classified as less than minimal even when clearing on the roentgenogram appears to be complete

Table 9-1. Bronchopulmonary Segments

RIGHT LUNG		LEFT LUNG	
LOBES	SEGMENTS	LOBES	SEGMENTS
Upper	Apical Posterior Anterior	Upper Upper Division	Apical Posterior Anterior
Middle	Lateral Medial	Lower (Lingular) Division	Superior Inferior
Lower	Superior Medial Basal Anterior Basal Lateral Basal Posterior Basal	Lower	Superior Anterior-medial Basal Lateral Basal Posterior Basal

* From *Diagnostic Standards and Classification of Tuberculosis,* 1950 Edition, with some re-arrangements of order of presentation

Location of Lesions. It may be useful to classify the extent of lesions in each lung separately. When this is done, however, the combined extent for both lungs should always be designated.

The location of lesions may be further designated by bronchopulmonary segments. The terminology and classification of Jackson and Huber * have been adopted upon the recommendation of the American Association for Thoracic Surgery.

CLINICAL CLASSIFICATION

The following definitions, subject to the interpretation of the physician, apply regardless of the type of treatment given Collapse therapy or pulmonary excision in effect at the time of classification will be indicated under extent of pulmonary lesions. The status of activity of lesions from a roentgenologic, symptomatic and laboratory standpoint is designated first, the status of a patient in terms of exercise shall be designated next.

Roentgenologic, Symptomatic, and Laboratory Status. *Inactive* Lesions as observed in serial roentgenograms must be stable except for extremely slow shrinkage, and there must be no roentgenologic evidence of cavity. Symptoms of tuberculous origin must be absent Sputum, if any, must be found negative for tubercle bacilli repeatedly, not only by concentration and microscopic examination, but also by culture or animal inoculation When a patient is not raising sputum or when there is any question concerning the authenticity or adequacy of expectorated sputum specimens, the fasting gastric contents or pulmonary secretions which have been aspirated from the tracheobronchial tree should be examined by culture or animal inoculation

These conditions shall have existed at least six months The period of inactivity shall be designated, if known, for example, Inactive (6 months), Inactive (2 years), et cetera.

Arrested. The symptomatic and roentgenologic requirements of this group are the same as for inactive, but the laboratory requirements are different.

When sputum specimens or gastric contents have been found negative by repeated microscopic examinations of concentrates but not by culture or animal inoculation, such patients cannot be classified as inactive but must be classified as arrested.

Patients may also be classified as arrested even though culture or animal inoculation may be positive and, among many concentrated specimens of sputum examined, an occasional positive is found microscopically

These conditions shall have existed at least three months The period of arrest shall be designated, if known, for example, Arrested (6 months), Arrested (2 years), et cetera

Active Lesions as observed in serial roentgenograms are usually progressive or retrogressive but may be stationary Symptoms of tuberculous origin are commonly present but may be absent Sputum and gastric contents almost always contain tubercle bacilli although, in some instances, tubercle bacilli cannot be demonstrated even after repeated cultures and animal inoculations With rare exceptions the tuberculin test is positive.

The period of activity shall be designated, if known, for example, Active (17 months), Active (3 years) The designations Active, Improved, or Active, Unimproved, may be used after an adequate period of observation or treatment.

Activity Undetermined When activity has not been determined from adequate roentgenologic and laboratory examinations, the disease must be designated temporarily as Activity Undetermined If a provisional estimate of the probable clinical status is necessary for public health purposes, the terms (a) Probably Active or (b) Probably Inactive should be used Every effort should be made to classify cases and to avoid this category

Exercise Status. The exercise status of a patient shall be designated:

I The patient is not ambulatory
II The patient has been ambulatory for less than one hour daily
III The patient has been ambulatory for one hour daily for a period of two months

* Jackson, C. L., and Huber, J. F. ... onchial Tree and ... Gray, Henry, in ... 1134-1135.

SCREENING CLASSIFICATIONS USED IN MASS ROENTGENOLOGIC SURVEYS. During the years the public has become conscious of the ravages of tuberculosis and has done much through sanitary methods in the home and by demanding purer milk supplies to control this disease. Those in charge of mass roentgenography seem to think that this method has been successful in the finding of many who have pulmonary lesions requiring further study.

As the use of this technic increases, the need for uniform standards and classification of screening-film findings becomes apparent The systematic terminology used by the National Tuberculosis Association which has proved to be practical and informative is presented here:

CLASSIFICATION OF PULMONARY TUBERCULOSIS *

Extent of Pulmonary Lesions. *Minimal.* Slight lesions without demonstrable excavation confined to a small part of one or both lungs The total extent of the lesions, regardless of distribution, shall not exceed the equivalent of the volume of lung tissue which lies above the second chondrosternal junction and the spine of the fourth or body of the fifth thoracic vertebra on one side

Moderately Advanced One or both lungs may be involved, but the total extent of the lesions shall not exceed the following limits·

Slight disseminated lesions which may extend through not more than the volume of one lung or the equivalent in both lungs.

Dense and confluent lesions which may extend through not more than the equivalent of one-third the volume of one lung

Total diameter of cavities less than 4 cm

Far Advanced. Lesions more extensive than moderately advanced.

Extent of Pulmonary Lesions Following Therapy. In the case of temporary collapse, the extent of disease existing immediately before the collapse shall be continued in the classification until re-expansion permits reclassification.

In the case of permanent collapse or pulmonary excision, the extent of disease in a lung existing immediately before excision or collapse shall be continued in this classification through life, except that such extension or new deposits of disease as appear any time postoperatively in this or the contralateral lung shall be additions to the preoperative classification. The form, site, and duration of the procedure shall be added in parenthesis to the classification of extent of disease

In other cases the classification of extent will be changed as the change in the extent of the demonstrable lesion warrants Once the diagnosis of pulmonary tuberculosis has been established, however, the extent of the lesion cannot be classified as less than minimal even when clearing on the roentgenogram appears to be complete

Table 9-1. Bronchopulmonary Segments

RIGHT LUNG		LEFT LUNG	
LOBES	SEGMENTS	LOBES	SEGMENTS
Upper	Apical Posterior Anterior	Upper Upper Division	 Apical Posterior Anterior
Middle	Lateral Medial	Lower (Lingular) Division	Superior Inferior
Lower	Superior Medial Basal Anterior Basal Lateral Basal Posterior Basal	Lower	Superior Anterior-medial Basal Lateral Basal Posterior Basal

* From *Diagnostic Standards and Classification of Tuberculosis,* 1950 Edition, with some re-arrangements of order of presentation

upon two factors: (1) the annual decrease of reactors to tuberculin among various age groups in the population; (2) the number of new cases and deaths reported annually that occur in families in which no tuberculosis has been known to exist previously. Careful observance of these two factors will give the best indication of the proper time for re-survey of any community or population group

DEMONSTRATION OF TUBERCLE BACILLI

The demonstration of virulent tubercle bacilli in the pulmonary secretions or gastric contents of patients with pulmonary disease is the one inescapable criterion of active pulmonary tuberculosis The results of other technical procedures, including roentgenologic examination, may be equivocal. However, if concentrated specimens from a patient are examined for tubercle bacilli by an expert at frequent intervals, the results, whether positive or negative, are of the greatest significance Since so much may depend upon a single sputum examination, certain precautions are necessary to make the examination as reliable as possible

Preparation of Glassware. All glassware used in sputum [collections and] studies must be scrupulously cleaned to ensure removal of any acid-fast matter which may adhere from previous use. Sputum bottles, after being autoclaved to ensure sterility, are held individually in a rapid stream of tap water to rinse out most of the organic matter The bottles are then boiled in soapy water for an hour, after which they are placed in cleaning solution for at least 12 hours to destroy any remaining organic matter. The cleaning solution is prepared by stirring 50 gm of technical-grade sodium dichromate into one liter of concentrated sulphuric acid (sp gr 1 82) After removal from this solution, the bottles are placed in a basin into which tap water is allowed to run rapidly for 30 minutes Finally each bottle is rinsed individually and dried and sterilized in an oven

Collection of Specimens. *Sputum* A wide-mouthed bottle of 30 to 300 ml capacity, cleaned as indicated above, should be used The bottle may have either a screw top or a snap cover The patient should be instructed to collect only secretion coming up the tracheobronchial tree from below the larynx, i e., not saliva or postnasal discharge. As used subsequently, the term sputum will refer only to secretion of this type coming from the lungs

Gastric Contents In certain cases, examination of the gastric contents for tubercle bacilli is essential. This is particularly true in children or other patients who do not raise sputum, as well as in patients whose sputum has failed to show tubercle bacilli after repeated examinations The technique of gastric lavage is as follows The material is collected after at least an 8-hour fast A Levine tube, carefully cleaned, sterilized, and lubricated with sterile water, is introduced through one nostril, the patient is asked to swallow as soon as he feels the tip of the tube in his throat With a glass syringe of 20 to 50 ml capacity, the gastric contents are withdrawn and placed in a sterile 250 ml. Erlenmeyer flask The patient is then given 30 to 50 ml of sterile water to drink, and the gastric contents are again aspirated and added to the first aspiration The specimen must be sent to the laboratory immediately and must receive the attention of the technician at once Prolonged standing may make the recovery of tubercle bacilli difficult or impossible Gastric specimens which must be sent through the mails may be frozen and shipped in dry ice It should be realized that, in the case of ambulant patients, a walk or long ride to the doctor's office may cause the stomach to empty before a gastric specimen is obtained

Other Clinical Specimens For the demonstration of tubercle bacilli in other body fluids, such as pleural, pericardial, or peritoneal effusions, spinal fluid, or pus from cold abscesses or sinuses, essentially the same methods are used as for sputum. . . .

To recover tubercle bacilli from urine, [at least] 1,000 ml taken from a well-mixed 24-hour specimen [is required]

Positive results from such voided specimens should be confirmed with catheterized specimens. These may be treated in the manner given above Also, it is advisable to inoculate the untreated sediment into guinea pigs.

In the examination of feces, [at least 5 gm. is required] . .

Negative Sputum. If sputums and gastric contents are carefully and repeatedly ve, negative results are of distinct diagnostic value. However, at a given specimen can never be called Negative for tubercle

IV. The patient has been ambulatory for at least two hours daily for a period of at least two months

V The patient is living under ordinary conditions of life.

The exercise status of a patient shall be designated following the designation of the roentgenologic, symptomatic and laboratory status; for example, Inactive (*6 months*) III.

Classification. Classifications of roentgenologic findings can be stated comparatively easily In summary, they may be listed as follows:

Screening Films of Any Size

1. Essentially *negative*
2. Unsatisfactory (technic)
3. Calcification only
4. Suggestive of tuberculosis
   a. Minimal
   b. Moderately advanced
   c. Far advanced

   Note *If* a provisional estimate is necessary, the terms probably active or probably inactive should be used for public health purposes
5. Suspected tuberculosis
6. Probably nontuberculous
   a Cardiac changes
   b Pleural changes
   c. Other changes
7. Diagnosis deferred

Explanation of Classification of Impression from Survey Films Following is a *brief* explanation of these classifications

1 Essentially negative. All apparently normal chests without evidence of present or past disease and without calcification

2. Unsatisfactory Technic unsatisfactory for screening, requiring retake

3 Calcification only (distinctly present in parenchyma or in hilum without infiltration)

4 Suggestive of tuberculosis Mottled, strand-like shadows especially in upper lobes, with or without evidence of cavity or associated calcification. The location and extent of abnormal shadows must be taken into consideration

a Minimal

b *Moderately advanced*

c *Far advanced*

5. Suspected tuberculosis Shadows of such character that opinion must be reserved until clinical studies can be made. This category includes such conditions as suspected hilar lymphadenitis, evidence of collapse therapy, and pleural effusion.

6 Probably nontuberculous. a Cardiac changes Abnormalities of size, shape or position of heart or aorta

b. Pleural changes Localized or extensive pleural thickening in the absence of other evidence of tuberculosis.

c. Other changes, such as tumors, silicosis, other pneumoconioses, or pneumonia

7. Diagnosis deferred Abnormal shadows not classifiable in the categories described above

Films regarded as suggestive of tuberculosis should be further qualified as (1) probably active or (2) probably inactive However, the diagnosis of tuberculosis and the estimate of clinical status of such cases should be provisional for all initial or screening examinations, even if the initial survey film is a 14 x 17 inch celluloid film

It should be emphasized that final diagnosis should *never* be made from survey roentgenograms alone, regardless of the technic employed One can be certain of exact diagnosis only after meticulous laboratory and clinical studies. Such studies should include clinical history, a physical examination, sputum examinations, gastric or tracheal cultures when necessary, tuberculin testing and serial roentgenologic examination The above classification, therefore, is for screening purposes only

Intervals for Re-Surveys. No arbitrary time interval can be recommended for re-survey of large population groups. The completeness of the initial survey, adequacy of isolation and treatment of newly-discovered infectious persons, and *follow-up* examinations of contacts of known cases will determine the need for or frequency of re-survey. Epidemiologically, the real test of the time interval of re-surveys will be based

of tuberculosis are, in the vast majority of instances, highly sensitive to PPD or Old Tuberculin. A dose of 0 00002 mg. of PPD or 0 01 mg. of Old Tuberculin is recommended for the initial dose for those living in areas having a high morbidity or mortality from tuberculosis, for those with a history of severe reactions following previous administration of tuberculin, for those with a history of intimate contact with persons with clinically manifest tuberculosis, and for persons with extrapulmonary forms of this disease.

If PPD is used, a standard product, which is available on the market, is dissolved in the requisite amount of the diluent supplied so that each 0 1 ml. of the dilution will contain 0.0001 mg of PPD To prepare the dose of 0 1 mg. of Old Tuberculin recommended for case-finding purposes, 0.1 ml of concentrated Old Tuberculin is added to 9 9 ml. of sterile physiological salt solution, thus making a dilution of 1:100. One milliliter of the 1:100 dilution of Old Tuberculin is transferred to 9 0 ml. of sterile physiological salt solution, thus making a dilution of 1.1,000 Each 0 1 ml of this dilution will contain 0 1 mg of Old Tuberculin Purified Protein Derivative and the diluted Old Tuberculin are best prepared fresh. Solutions more than a few days old should not be used When not in use, diluted solutions should be kept in a refrigerator.

For the present, with certain exceptions as noted, the use of a single dose is recommended Further studies on the specificity of the larger doses of both PPD and Old Tuberculin are being made

The intracutaneous tuberculin test (Mantoux) with either PPD or Old Tuberculin should be read 48 or 72 hours after the injection Readings should be made in a good light with the arm slightly flexed Response to injection is classified as positive, negative, or doubtful. Reactions may be classified arbitrarily as one, two, three or four plus depending upon the extent of induration measured at its widest diameter. A reaction showing some definite induration more than 5 mm and not exceeding 10 mm. in diameter is recorded as a one plus (+) reaction A two plus (++) reaction is an area of induration measuring from 10 to 20 mm in diameter. A three plus (+++) reaction is characterized by marked redness and induration exceeding 20 mm. in diameter A four plus (++++) reaction consists of severe induration and an area of necrosis. A reaction with a trace of induration measuring 5 mm. or less in diameter is rated as doubtful Redness without associated induration does not constitute a reaction.

Syringes which have been used for the administration of PPD or Old Tuberculin should not be used for the administration of preparations such as coccidioidin, histoplasmin or other diagnostic reagents since PPD and Old Tuberculin are difficult to remove from the syringes

Scarification or Pirquet Test This procedure is carried out by applying a drop of undiluted Old Tuberculin to the cleansed skin, preferably over the region of the deltoid muscle, and scarifying the skin through the drop of tuberculin by means of a sterile needle or small borer Care should be taken that the scarification does not cause bleeding. The tuberculin should be permitted to remain in situ for about 20 to 30 minutes before the excess is removed The results of the test are read 48 to 72 hours later and are interpreted in the same manner as the intracutaneous test. If there is no tuberculin reaction by this method, it is advised that it be followed by the administration of 0 0001 mg of PPD or 0 1 mg of Old Tuberculin, using the intracutaneous method.

Patch or Percutaneous Test of Vollmer The patch test is carried out by applying a prepared patch to the skin in the region of the sternum or between the scapulae. The patch is composed of two squares impregnated with concentrated tuberculin prepared from cultures grown on a synthetic medium and one control square impregnated with [illegible] n is first cleansed with acetone and the patch [illegible] 48 hours The reaction is read 48 hours after [illegible] ears as an inflamed area of varying intensity. In those highly sensitive to tuberculin, it is advisable to remove the patch as soon as the person complains of irritation since a severe local reaction with blistering may occur. If the patch test is negative, 0 0001 mg of PPD or 0.1 mg of Old Tuberculin should be injected

Of the procedures here described, the intracutaneous method is the most sensitive and permits the administration of graduated and accurate amounts, thus making it

bacilli until it has been examined by adequate cultural methods and animal inoculation as well as by examination of the direct and concentrated smears In a patient with a demonstrable parenchymal infiltration, in whom tubercle bacilli cannot be demonstrated, causes for the lesion other than active pulmonary tuberculosis should be sought.

In a tuberculous patient no specified number of negative sputum examinations gives absolute assurance that another specimen may not show tubercle bacilli. Nevertheless, it is convenient to designate an arbitrary number of negative examinations which may be taken as presumptive evidence of bacteriologic remission. To designate sputum as negative in this limited sense, it is recommended that three adequate specimens of sputum or of gastric contents, taken at least a week apart, be found negative by culture or by animal inoculation

TECHNICAL PROCEDURES

The Tuberculin Test. The tuberculin reaction is an acute, local, specific inflammation resulting from the injection or application of tuberculin. Few procedures employed in the control of tuberculosis are of greater value than the tuberculin test As an index of the extent of infection in communities, it is of the utmost epidemiological value It locates sources of contagion and provides a guide for case finding and family and group supervision. Its importance in the diagnosis of tuberculosis rises constantly as the rate of infection in the population decreases and as the total number of cases of active disease declines Whereas its value in clinical diagnosis once was exclusive rather than definitive in character, the tuberculin test is becoming a more positive indication of significant infection Finally, with the expansion of BCG vaccination programs and the importance of determining the relation of artificial infection with an organism of low virulence to the development of individual resistance, the tuberculin test has become of special significance as an indication of the take of the vaccine

Obviously, once BCG has been administered, the tuberculin test loses its specific value as an indicator of natural infection

A reaction to certain specified amounts of tuberculin is an indication of tuberculous infection With few exceptions, definite sensitivity to tuberculin once acquired persists through life This sensitivity may vary in intensity and may temporarily decrease or disappear in the course of high fever, exanthematous disease, miliary tuberculosis, and the last stages of pulmonary tuberculosis A very small percentage of persons may fail to react to tuberculin even after infection resulting from exposure to cases of open tuberculosis or after the administration of vaccine prepared from living or dead tubercle bacilli. The tuberculin test remains negative in a high percentage of cases of sarcoidosis

At the present time Purified Protein Derivative (PPD) and Old Tuberculin (OT) are widely used Purified Protein Derivative (PPD) is the tuberculin of choice and is recommended as the standard for comparative studies. It is prepared by growing tubercle bacilli on a synthetic medium of known composition. The tuberculin protein produced in the medium is then obtained by precipitation with ammonium sulfate at neutrality and further purification. Old Tuberculin is prepared by concentrating by heat the glycerine broth medium upon which the tubercle bacillus has grown

TECHNIC The method of choice in administering tuberculin and the one recommended for accuracy and for all general purposes is the intracutaneous (Mantoux) test Occasionally, however, special circumstances may make other methods of administration preferable. In the following paragraphs the intracutaneous method is described as the standard procedure A description is also given, however, of the scarification (Pirquet) test and of the Vollmer patch test, which is frequently employed when there is objection to the use of a needle Neither of these tests is considered as accurate as the intracutaneous test, in which a measured amount of tuberculin is introduced into the skin

Intracutaneous or Mantoux Test The intracutaneous tuberculin test is best carried out by injecting the desired concentration of PPD or Old Tuberculin into the cleansed skin of the forearm. This injection is made with a short (half inch), sharply beveled 24- or 25-gauge platinum or steel needle and a tuberculin syringe. When the injection [illegible] immediately at the site of injection

[illegible] or 0.1

[illegible] recom-

[illegible] teristic

mended since [illegible]

diagnosis of such diseases must depend on laboratory studies of materials obtained from patients, including direct microscopic examination of sputum, cultures of sputum, pathogenicity tests of organisms isolated, and sensitivity and serologic tests. *Actinomyces bovis, Nocardia asteroides, Candida albicans, Geotrichum candidum* and *Histoplasma capsulatum* are best detected in stained smears of the sputum (see Chapter 17).

India ink preparations are used to demonstrate the capsule which surrounds the budding, yeastlike cells of *Cryptococcus neoformans.* A medium containing penicillin and streptomycin supports the growth of pathogenic fungi with two exceptions, *Actinomyces bovis* and *Nocardia asteroides,* which are susceptible to penicillin and streptomycin and must be cultivated on other mediums Most fungi known to cause pulmonary infections are pathogenic for one or more laboratory animals such as mice, rabbits and guinea pigs Many patients with fungous infections manifest sensitivity to the invading organism or its products, and intradermal injec- [illegible]

[illegible]

positive serologic reaction in coccidioidomycosis, histoplasmosis and blastomycosis, in which the complement fixation tests have been used most extensively, is indicative of an active, progressive disseminated infection Such a test is therefore diagnostic. Cross reactions are known to occur between *Blastomyces* antigens and antiserum against *Histoplasma capsulatum.* Any serum tested should be tested against both *Blastomyces* and *Histoplasma* antigens

TUBERCULIN, COCCIDIOIDIN AND HISTOPLASMIN SENSITIVITY IN RELATION TO PULMONARY CALCIFICATIONS In view of the evidence that histoplasmosis and coccidioidomycosis may be etiologically associated with pulmonary calcification, Beadenkopf and associates included these antigens among the skin tests given as part of the tuberculosis control program at the University of Chicago Only 30 per cent of the students enrolled came from Chicago and vicinity, the greater number came from practically all parts of the United States, and several hundred were from foreign countries The report was based on the study of 6,000 students registered at the University from January 1 to October, 1947 This study on a population of diverse origin confirms the results of other recent surveys. It was found that (1) the prevalence of tuberculin sensitivity progressively increased from 10 per cent among the youngest age group to 57 per cent among those 50 years of age; (2) the rate of histoplasmin sensitivity began at 10 per cent among the youngest group and reached 38 per cent in the oldest group, (3) pulmonary calcifications were associated with histoplasmin sensitivity twice as frequently as they were with tuberculin sensitivity, and (4) the prevalence of both histoplasmin sensitivity and pulmonary calcifications [illegible]

[illegible]

by tuberculin cutaneous testing In this area from one third to four fifths of young persons have pulmonary calcification Only one half or less of those who have pulmonary calcification have positive tuberculin reactions.

Anergy or loss of sensitivity to tuberculin from complete healing of the tuberculous process may be an acceptable explanation in some instances but this cannot explain the decided prevalence of pulmonary calcification in this area.

Cox and Smith, Aronson, Saylor and Parr and others have shown that in certain areas of the West coccidioidomycosis is responsible for a primary complex which goes on to calcification. The suggestion of Smith that histoplasmosis occurs most frequently in the area where pulmonary calcification is high in those whose reaction to tuberculin is negative seemed to offer a good working hypothesis

possible to detect cases with a low threshold of sensitivity to tuberculin. The general use of the Pirquet and the patch test is not recommended since they are not so efficient as the Mantoux test

Methods of Case Finding in Tuberculosis. The facilities used in case finding have continually been improved. At first the only means of finding tuberculosis was by physical examination; then came the discovery of the bacilli and the use of the microscope, and then the roentgen rays Following this the tuberculin test was applied with much success, and finally the miniature roentgenogram was developed

The mass roentgenologic survey method in large communities is probably most effective and cheapest, this is true especially of the 70 mm. machine, which may be used with all the facility of the earlier developed 35 mm., and yet possesses most of the advantages of the larger (14 by 17 inch) films The cost is not large, and the results are probably of more direct value than those obtained with any other method. The roentgenologic method finds the significant lesions which can be quickly treated.

Several things roentgenologic surveys do not do. Since roentgen shadows are not specific they are not pathognomonic of tuberculosis. Subsequent sputum analyses and tuberculin tests are necessary in 3 to 5 per cent of all cases surveyed, often revealing that conditions which at first were called tuberculosis actually are some other disease Second, the roentgen rays will not always reveal the presence of tuberculous lesions, since about 30 per cent of the chest area is hidden, and since many early lesions do not cast shadows.

The tuberculin test method, as introduced by Opie, Long, Meyers and a large number of others, has many advantages not possessed by any other technic. A tuberculin test helps to rule out nontuberculous disease. When the reaction is positive in infants and young children and even in young adults, the test is a certain indication of proximity to open tuberculosis. Because more persons will reach adult life in the future without infection, the test will become increasingly useful

One of the greatest benefits of tuberculin testing in survey work is found in communities where only 30 per cent or less of the population has a positive tuberculin reaction Obviously the majority of the roentgenograms of those with negative tuberculin reactions would be wasted The tuberculin method in such circumstances should be used first and followed by roentgenograms of the positive reactors Finally, when used fully, the tuberculin test is perhaps the best index of the efficiency of a tuberculosis control program in any community.

The tuberculin survey method is the most practical in communities where the infection rate is low Positive reactors may be given roentgen examinations after a tuberculin survey on entering and on leaving school. Follow-up of all contacts should be made and health education intensified.

In larger communities where the infection rate is high, probably the best method is to give roentgen examinations to everybody more than 15 years of age and the tuberculin test to all those with suspected lesions. Although a few small lesions will escape the roentgenologic survey, the number will not be of great importance The cost of each method when used in its respective proper setting is probably about the same, based on the total cases surveyed The roentgenogram is cheaper per number of cases found and number of deaths from tuberculosis, while the tuberculin test method is more useful in small communities and is, above all, a sound index of the control of the disease These two principal methods should and do supplement each other, the choice and sequence depending on time, place and available facilities.

Differentiation of the Active Phases of Pulmonary Mycosis and Tuberculosis. *Actinomyces bovis, Nocardia asteroides, Coccidioides immitis, Blastomyces dermatitidis, Blastomyces brasiliensis, Histoplasma capsulatum, Cryptococcus neoformans, Candida albicans* and *Geotrichum candidum* cause subacute and chronic infections of the lungs which resemble tuberculosis These diseases often cannot be separated and never can be definitely diagnosed on clinical findings alone The incidence of these mycotic infections is as a rule low in comparison with the incidence of tuberculosis. In the absence of positive smears, cultures and guinea pig inoculations for tuberculosis these mycotic diseases should be considered The

it is certain that no outside contact has been made within a year, there has never been during the residence of foreign observers in these communities the slightest evidence of acute infections of the respiratory tract Let there be contact with outsiders, and these communities will have an epidemic of colds within 2 days. It must be emphasized, however, that despite the studies which have been made in these communities, in reality the number of studies has been small and the time spent in these localities by investigators has been for practical purposes too short to establish the conclusions which have been reached.

From the data now obtainable it seems likely that a virus is present in the nasal discharge of patients during the first 3 or 4 days of an attack of a viral cold. This virus, when dispersed in the air or on objects in the open air, remains infective for about 5 hours The virus is said, too, to be spread by contaminated hands, either directly or indirectly. Likewise drinking glasses, cups, forks and spoons are excellent vehicles for the transmission of the cold virus, as well as other germs, from one person to another However, it has not been proved that colds are thus epidemically disseminated

INCIDENCE. Colds are more prevalent during the winter months than in other seasons in both *cold and temperate climates.* They seem to go around several times during the winter months of each year.

The prevalence of colds is about the same in the agreeable climates and the disagreeable climates Sleeping on sleeping porches, in well-ventilated bedrooms, or in poorly ventilated bedrooms does not affect individual susceptibility

During the winter months of each year there is a tendency for colds to increase when there is a decrease in temperature below the normal range of temperature for the corresponding week and also for the preceding week.

ETIOLOGY Among the various etiologic agents which deserve mention are viruses, bacteria, chilling, physical agents, allergies and climate.

Viruses. Dochez and his associates concluded that colds can be transmitted from man to the chimpanzee and from man to man by means of Berkefeld filtrates of nasal washings from individuals suffering from acute colds, and that the cause of colds is "a filtrable agent which in all likelihood belongs to the group of so-called submicroscopic viruses " The conclusion seems justified that a filtrable virus is the cause of certain colds and probably of some epidemics but not all of them.

Bacteria Colds of bacterial origin begin with a severe sore throat with the nasal discharge and congestion appearing later as the infection extends upward into the nasal passages. It seems that bacterial colds may appear in the course of a viral cold, and are probably due to secondary bacterial invaders. The vasomotor reaction may so disturb the equilibrium between the host and the bacteria of the nose as to favor the development of infection

Allergies The symptoms which allergens produce in the upper portion of the respiratory tract are essentially those of an acute coryza However, there seem to be regularly, each year, the so-called spring and fall colds in addition to these allergic phenomena

Physical Agents These include climates, good or bad, chilling of the body, and injury of the mucous membranes by particulate matter.

The exposure of an individual to drafts and *chilling of the whole or of portions of the body* may result in the symptoms of a cold It has been demonstrated that chilling of the body surfaces leads to peripheral vasoconstriction with attendant peripheral stasis and anoxemia, to lowered leukocyte response, and to impairment of the phagocytic capabilities of the fixed tissue cells, including those of the nasal mucous membrane Chilling of the body surfaces causes a fall in the temperature of the nasal and pharyngeal mucous membranes, and this chilling and the accompanying congestion increase susceptibility to a cold

The occurrence of colds in different geographic locations has illustrated that the attack rates are uniform, irrespective of latitude, longitude, or climate. The period of high incidence and the occurrence of epidemics in widely different localities often take

Christie and Peterson accordingly began to perform cutaneous tests with extracts of *Histoplasma capsulatum* and to look for nonfatal examples of the infection. The fungus *Histoplasma capsulatum* had been reported to cause acute and subacute granulomatous lesions progressing with great regularity to a fatal termination Their studies enabled them to observe examples of a benign form of histoplasmosis and to discover that many people react to extracts of the fungus.

The studies of Christie and Peterson and of Palmer and Furcolow show a remarkable relationship between sensitivity to histoplasmin and the development of pulmonary calcification. The early development of sensitivity to histoplasmin, followed by the development of the calcification at a rate much greater than the age specific rate of sensitivity to tuberculin, suggests that most of the lesions are more likely to be related to the development of sensitivity to histoplasmin than to be associated with tuberculosis.

According to Aronson and his co-workers, Indians of the United States and Alaska who failed to react to the intracutaneous injection of 0.00002 and 0.005 mg of Purified Protein Derivative of tuberculin revealed calcified pulmonary nodules Among 704 children living on the Pima Agency who did not react to tuberculin, calcified pulmonary nodules were observed in 102; among 419 on the Wind River Agency only 1 of those who failed to react to tuberculin had a calcified pulmonary nodule, among 332 children living on the Turtle Mountain Agency who did not react to tuberculin, 15 had calcified pulmonary nodules, and among the 592 children of the Rosebud Agency and the 977 children living in southeastern Alaska who failed to react to tuberculin 6 and 2 presented calcified pulmonary nodules Because of the high incidence of calcified pulmonary nodules in tuberculin negative children living on the Pima Agency the possibility that the nodules were coccidioidal was investigated A large percentage of children of school age living on the Pima, San Carlos and Sells agencies and a small percentage of those living on the Fort Apache Agency reacted to the injection of 0.1 ml of a 1:1,000 dilution of coccidioidin.

DISEASES OF THE RESPIRATORY PASSAGES AND THE LUNGS DUE TO FILTRABLE VIRUSES

The Common Cold. The consensus is that the common cold and its complications in the United States are the cause of more illness and disability than any other illness It must be clear that the term cold is applied by the physician and laity alike to various acute, subacute, and even chronic maladies of both the upper and lower portions of the respiratory tract, and thus statistical data concerning the incidence and the duration of the common cold are well-nigh impossible to interpret The term coryza refers to a cold in the head.

An acute respiratory infection often does not remain limited to any one portion of the respiratory tract For instance, rhinitis today may become sinusitis, pharyngitis, laryngitis, tracheitis or bronchitis tomorrow. In many instances the sequence may be changed, partially at least Tracheitis, laryngitis or pharyngitis may be largely over in a day or two, to be followed by rhinitis In reality, many individuals regularly with each cold have symptoms which commence as pharyngitis, laryngitis or tracheitis, to be followed by coryza.

EPIDEMIOLOGY. Colds are cosmopolitan in distribution in regard to geography, altitude and age incidence The attack rate is highest and the complications are most frequent and most serious in infants and in the aged. From these ages the rate declines to a low point in the age group 15 to 24 years, rises from 25 to 34 years, again declines until it reaches a minimum in the age group of 50 to 60 or 65 years and then tends to increase.

ISOLATION Some extraordinarily interesting observations on the occurrence of colds have been made in isolated communities. In the arctic and polar regions, when

respiratory tract such as laryngitis, tracheitis, bronchitis and pneumonia. Closely allied to colds are the diseases influenza and tonsillitis

It is postulated that complications of the common cold may occur when drainage from the sinuses or middle ear is obstructed by swelling of the mucous membranes. The presence of virulent organisms in the nose and throat at the time of the cold is likely to originate disease when the subject is in poor health.

DIAGNOSIS. The diagnosis of a common cold is a presumptive one until the patient has fully recovered The diagnosis of a complication of a bad cold depends on the excessive localization of symptoms and signs to the sinuses, ears or lungs. It is well to recall that some of the aches in the back, muscles and head are due to fever. Anorexia is due to loss of the senses of smell and taste Constipation is occasioned by lack of food In some instances diarrhea may be due to cold remedies which have been self-administered

Influenza. Influenza is known also as grippe, grip, febrile catarrh, catarrhal fever, acute nasopharyngitis, epidemic catarrh and epidemic influenza.

Influenza is an acute, self-limited, infectious disease of man which is caused by a virus of the influenza group. The illness is characterized by symptoms which are predominantly constitutional, although the infection is limited to the respiratory tract. It tends to occur in epidemic forms Two specific and distinct etiologic types of the disease are now recognized one, termed influenza A, is caused by infection with influenza A virus, the other, termed influenza B, is caused by infection with influenza B virus (Horsfall, 1940) The cause of pandemics of influenza has not been established

Among the periodic outbreaks of influenza the major ones are apparently due chiefly to influenza A virus, others may be due wholly or partly to influenza B virus; still other viruses may produce morbidity but may fail to show signs of their presence, although the illnesses produced by these as yet unproved viruses are clinically like those of known influenza A and B viruses Influenza A virus varies from one outbreak to another, antigenically, and in its rapidity of spread in the population. Influenza B virus produces epidemics of limited scope Influenza A virus usually lies quiescent for 21 months out of 24 During this quiescent interval there is some relationship between the individual immunity and the level of neutralizing antibodies in the serum

Influenza viruses may vary greatly from one epidemic to another. As an example of the variability of the influenza virus, according to Tamm, Kilbourne and Horsfall the influenza B virus isolated in the New York area during the 1950 epidemic was so different from previous strains as to throw doubt on the desirability of continuing the use of a routine strain exclusively in prophylactic immunization Using the chick embryo technic, four strains of influenza B virus were isolated from hospitalized patients Tamm, Kilbourne and Horsfall had for comparison the routine virus and five strains isolated by the same technic during previous epidemics (1945, 1947, 1949). Thus it is possible that it will be necessary to use a polyvalent influenza B vaccine in the future rather than to depend on the Lee strain exclusively.

Influenza viruses are not known to be related to the etiology of the common cold

EPIDEMIOLOGY The consensus is that a primary epidemic occurring in any locality after a period of years nearly free from the disease, is a uniform disease Influ [illegible]

[illegible]

decr [illegible]

The fatality rate, although variable, is low.

Primary epidemics are followed by secondary epidemics which are less extensive and more slowly reach their maximum, from which they decline more slowly and irregularly. Because of secondary pulmonary complications, the fatality rate is greater in the secondary epidemics than in the primary epidemic.

Influenza regularly occurs in endemic or seasonal form in most countries every

place synchronously, too fast for human travel and thus transport of the offending etiologic agent.

Temporary irritation or injury of the membranes of the nose and throat by *particulate matter* such as various dusts will cause the nasal symptoms characteristic of colds If the exposure to irritation is prolonged, the symptoms may subside or may become chronic and severe Smoking of cigarettes may be a factor in keeping up a low-grade *chronic irritation* Irritating chemical gases or air filled with particulate matter (dusts) or overheated dry air predisposes to colds

Indeterminate differences in individual susceptibility to colds cannot be explained

Some individuals seem to have hypersusceptibility to the common cold. Others are rarely susceptible to colds under any circumstances. These variations cannot be adequately explained by hypersensitivity due to an allergic state, or by immunity.

In persons who have frequent colds the vasomotor response of the nasal mucous membranes to peripheral cold stimuli is much less in degree and slower in appearance than in normal persons, and during an acute cold this reaction is entirely absent

Persons who are taking active physical exercise and who have accustomed themselves to rapid changes in temperature are less susceptible to colds than other persons even if they have the foredescribed mucous membrane attributes.

SYMPTOMS. The common cold commences in one or more of several ways. Often the first symptom is a feeling of congestion in the nose with sneezing Other colds will begin first with a general ache and perhaps slight fever, the temperature from 99 to 100 F (37 2 to 37 7 C), and still other colds will be accompanied with general aching, malaise, and loss of appetite for a day or more before there are any respiratory symptoms. Once any one or all of these discomforts are established, symptoms in the nose and throat ensue There is localized or generalized burning in the nose and throat. The discomforts spread and the mucous membranes of the nose, nasal sinuses and pharynx become red and swollen As the result of swelling of its mucous membranes, the nose becomes obstructed so that mouth breathing is more comfortable than nose breathing If the sinuses are prevented from draining by the swelling, there is a dull ache in the face and head The inflamed mucosa secretes a watery, serous exudate which drips almost constantly from the nose. This watery secretion is irritating to the outside skin of the nose and the upper lip.

The inspiration of cold air, dust or tobacco smoke hurts the nasal passages. Often confirmed cigarette and cigar smokers cannot tolerate their favorite pastime because the smoke hurts the nose and throat and may make the headache worse Involvement of the eustachian tubes causes noises created by the mucus and air in the tubes to be heard as popping and roaring sounds in the ears. If the eustachian tubes become closed, temporary deafness follows. The throat becomes dry, swollen and uncomfortable The tongue is dry. The senses of taste and of smell are impaired or lost A decrease in the degree of the acuity or a permanent loss of either or both the senses of smell and taste may follow a cold. However, recovery of the senses (hearing, smell and taste) is almost invariably the rule.

Slight fever may accompany acute colds A moderate or a high fever, the temperature more than 102 F (38 8 C), indicates more than a cold, for instance, some complication such as sinusitis, otitis media, tonsillitis, bronchitis or pneumonia

Involvement of the lower part of the respiratory tract with hoarseness and coughing is commonly present in some individuals; in others it rarely occurs.

EXAMINATION. Examination by physical means reveals the linings of the nose, the pharynx and throat to be reddened. The voice often is husky or lost Nasal or labial herpes may be found. If the mucous membranes of the tear ducts are swollen, the eyes are watery and the conjunctivae are injected. The lungs are clear.

An important reason for a complete physical examination of the patient who has a bad cold is to search for evidence of complications The complications of colds are sinusitis, otitis media, and more than transient infections of various parts of the

pneumonia of influenza is generally combined with capillary bronchitis upon which it supervenes. The instances in which pneumonia is combined with bronchitis are less commonly fatal than those in which capillary bronchitis alone existed.

Gastrointestinal Form This form of influenza begins with severe colicky pains, vomiting, and diarrhea. In this form, and in the nervous form, the catarrhal symptoms are often altogether absent, or only come on late in the course of illness.

Nervous Form The nervous form is characterized by intense headaches and backache. The backache may be as severe as that which occurs during a hemolytic crisis or in smallpox The headache, frontal, in some cases occipital, and occasionally vertical, is often persistent, continuing for some days after the patient's temperature has subsided to normal values.

The nervous form of influenza occurring in tropical and subtropical regions may be difficult to differentiate from dengue (six day fever, breakbone fever) except by laboratory tests.

SYMPTOMS. The onset of influenza is sudden On this point all of those who have reported the epidemics which have occurred from remote to recent times have agreed

Fever is constantly present except in cases in which pronounced nervous symptoms exist. The temperature may reach high figures, 105.8 F (41 C) early in the course of the disease, but if defervescence is rapid no great harm is done. The fever lasts from 3 to 10 days; the longer the fever continues, the more likely it is to resolve by lysis.

Coryza or *rhinitis*, or both, vary greatly in different epidemics of influenza. In most instances there is some degree of involvement of the respiratory system. In the total number of persons who have the disease these symptoms are not severe. The respiratory rate is usually not increased unless there are pulmonary complications. An early increase in the respiratory rate is an ill omen

Cough is not always a prominent feature, and often it is absent. The cough bears but little relation to the extent of the physical signs in the lungs. It is likely to occur in paroxysms which are sometimes very exhausting Toward the end of the grave illnesses cough, which may have been very troublesome indeed in the earlier stages, generally ceases, even though the lungs are full of rhonchi and rales

Pain may be the earliest symptom of influenza. Pains in the limbs and back, shivering, and often severe headache may be the only symptoms for a day and a night. The pains are referred almost invariably to the muscles and soft tissues, and to a less extent to the joints rather than to the bones themselves The commonest sites of pain are in the muscles of the thighs and calves, the lumbar muscles and muscles of the back of the neck, and to a less extent the knees and ankle joints. The pains are severe but differ considerably from those of trench fever and smallpox In these diseases the pains are most frequently referred to the bones themselves, particularly to the inner and outer edge of the tibiae, and the bones are often very tender to palpation The acute nocturnal exacerbations of the pains are more marked in trench fever than in influenza

The abdominal pains in some of those who have influenza are more general, and [illegible]

not tend to become localized, and the fever and pulse rate do not indicate a progressive lesion

There are those who have occipital headache and pain in the neck closely resembl [illegible]
is muc [illegible]
sign is [illegible]
a true Kernig's sign Lumbar puncture may, however, be necessary to exclude cere-

year. The exact relationship of endemic influenza to the classic pandemic type of influenza is unknown. Many believe that endemic influenza and the minor outbreaks are a repetition of the classic type, but during a period of attenuation of the virulence of the virus; others suggest that endemic or sporadic influenza is an infection of a different nature or type altogether.

The frequency of the outbreaks of influenza and its tendency to reach pandemic proportions, affecting equally those of all economic and social levels of society, traveling from continent to continent at a speed equal to that of human travel, affecting and destroying millions of lives (the 1918-1919 pandemic with 21,642,283 deaths), respecting no barriers set up for control by public health organizations, and leaving behind ill health and disease, stigmatize influenza as the greatest pestilence of our time The importance of this disease, in addition to its own morbidity, lies in its power to induce a condition of particular susceptibility to attack by secondary pathogenic organisms, particularly the hemolytic streptococcus and tubercle bacilli

The pneumonia which often follows influenzal infections is caused by an associated bacterial invasion of the lungs In cases of *Staphylococcus aureus* pneumonia complicating sporadic instances of influenza, the staphylococcus is present in almost pure culture. The hemolytic streptococcus (type A) is more commonly present in the various epidemics of pneumonia following influenza. The pneumococci and *Hemophilus influenzae* may be the bacterial agents responsible for some of the pulmonary complications It seems reasonable that the influenza virus itself may be capable of originating bronchopulmonary reaction if not an actual pneumonia The diffuse bronchiolitis which may occur after epidemic influenza may represent a true viral lesion of the lung.

The effect of endemic influenza on the morbidity as well as on the mortality rate from pneumonia and tuberculosis, and on the birth rate is less marked than that of the pandemic disease Prevalence of endemic influenza is more influenced by seasonal conditions as compared with the pandemic type

PATHOLOGY. The evidence would indicate that the filter-passing virus of influenza gains access to the body by the respiratory tract. The influenza virus injures or *destroys the ciliated epithelium lining the air passages.* It inflicts an initial damage of the epithelium of the respiratory tract at special selective sites In this respect stress is laid on the importance of the postnasal area as an important pr[illegible] infection in the body From this area the virus may [illegible] severe damage in the ciliated epithelium in the lowe[illegible] importance is laid on the very frequent occurrence of tracheitis in influenza, since destruction and damage to the delicate ciliated epithelium in this area cause the disappearance of an effective barrier to invasion of the lungs by inhaled bacteria, thus offering an explanation for the great frequency of secondary invasion of the lungs in influenza

The virus may invade the lungs by indirectly gaining access from the congested pharyngeal veins and extravasated blood in the submucosa of the postnasal region, by traveling in the form of minute infective emboli along the arterial route, and may become arrested in the terminal arterioles of the pulmonary artery.

CLINICAL VARIETIES. The clinical varieties of influenza are separated according to the manifestations of the disease. They are. (1) simple catarrhal fever, (2) pulmonary form, (3) gastrointestinal form and (4) nervous form.

Simple Catarrhal Fever. The usual early symptoms are a feeling of tightness and constriction in the thorax, disappearing with the onset of cough and expectoration Rales and rhonchi may be heard in auscultation The simple form tends to be remittent in character, the symptoms usually abating in the daytime and increasing in severity toward evening Great prostration attends the disease throughout its course, and may last for days or weeks after convalescence.

Pulmonary Form The sense of constriction in the thorax, dyspnea and stiffness, and soreness in the throat are much more intense than in the simple form The

Confirmation of the clinical diagnosis of influenza may be obtained by the demonstration of a rise in the antibody titer of serum collected during convalescence as compared with serum obtained early in the illness and by isolation of virus from nasal or pharyngeal washings It seems that many laboratory workers prefer the agglutination-inhibition test. This test is based on the fact that influenza viruses agglutinate chicken red blood corpuscles and that this capacity is specifically inhibited by immune serum

Less than a fourfold antibody response formerly was considered within the limits of experimental error The frequent occurrence of twofold increases in titer in the agglutination-inhibition test may be considered indicative of influenzal infection. However, this or any other laboratory test is not available for general diagnostic use in influenza

Differential Diagnosis There are certain types of influenza in which it is often extremely difficult to come to a diagnosis because of their marked resemblance to other infections.

Since conjunctivitis, laryngitis, bronchitis, tonsillitis and frontal headache are common to *measles* and influenza, a certain diagnosis may not be possible before the fourth day, when the fresh febrile accession and the appearance of the rash indicate measles.

Owing to the acute onset, with shivering and cough, influenza may bear a close resemblance to *central pneumonia*, from which it can be distinguished by roentgenoscopic examination of the lungs

If the attack of influenza commences with gradual pyrexia, with diarrhea, rose spots, and enlargement of the spleen, as happens occasionally, in both *typhoid fever* and influenza, the diagnosis may have to wait until the temperature begins to fall, on the third or fourth day of the illness, when the disease is recognized as influenza. Leukocytosis is absent in both diseases when uncomplicated

There is often difficulty in the differential diagnosis between the abdominal type of influenza and *acute appendicitis* In acute appendicitis there are increasing numbers of leukocytes, whereas in influenza the leukocytes are normal or decreased in number In the absence of a significant leukocyte count, the appendicular form of influenza may resemble acute appendicitis so closely as to render a correct diagnosis impossible without a period of observation too long to be safely carried out.

Primary Atypical Pneumonia. This disease, though it occurs as frequently in the older age groups as in the younger, has been the subject of written reports chiefly because of its incidence among young adults in schools, colleges and army camps

Etiology and Epidemiology A viral etiology for atypical pneumonia has been implied by the exclusive methods practiced by bacteriologists By appropriate methods materials consisting of washings from the noses of selected subjects suffering from primary atypical pneumonia have been transferred to healthy individuals These healthy individuals in due time have manifested respiratory illnesses varying in severity and clinical manifestations corresponding to those of atypical pneumonia

Epidemics of viral pneumonia occur in the fall and winter. The disease does not seem to be highly communicable. There are numerous instances, however, of contact infection from patient to nurse and from one member of a family to another. These observations suggest that often prolonged and intimate contact with patients is necessary for infection. The incubation period is from one to two days No difference has been observed in the susceptibility of the sexes

Pathology Necropsy has revealed patchy hemorrhagic bronchopneumonia with acute bronchitis and bronchiolitis

Symptoms The onset is with a cold or sore throat and cough and chilly feelings, but rarely a chill The cough is at first a dry cough. A pain through the anterior and midportion of the thorax is almost always present. The headache increases in intensity and persists throughout the febrile period The fever tends to be of an irregular type with one or two rises within the 24 hours The temperature peaks

brospinal meningitis, when, although the fluid may escape under high pressure, it is clear and does not present the characteristic cytologic features of the latter disease

Substernal pain, varying from a mild soreness to acute pain, is often associated with influenza

In the earlier stages of an epidemic, progress is rapid, and convalescence is usually established on an average of 5 days without any sequelae Later in an epidemic, both the intensity and the virulence of the disease increases, convalescence is more protracted as the febrile period lengthens, and the bronchitic infections are more pronounced

A high temperature is not a grave symptom during the first 48 hours of influenza Unfavorable symptoms are delirium, stupor, insomnia, persistent vomiting and severe diarrhea

EXAMINATION A bright flushing of the cheeks is common at the commencement of the disease

A light cyanosis is often observed on the cheeks, lips, ears and neck. This coloration is distinctly different from the darker cyanosis commonly seen in pneumonia or bronchitis In those who have capillary bronchitis it may become evident before the development of signs in the lungs

As a peculiarity in influenza, *sweating* was observed in early times, and the "sweating sickness" in the sixteenth century may have been a virulent influenza The profuse perspirations occur during the febrile period and may give rise to a curious odor, which is said to be similar to that of typhus patients Profuse odoriferous sweating is most often present in very ill patients who have influenza and must be regarded as an unfavorable symptom.

A diffusely distributed *erythema* has often been observed *Purpura* may be present as a terminal event Herpes labialis and redness and suffusion about the eyes vary in degree in each case.

A relative *slowness of the pulse* is often a common feature while the fever is at its height A sudden rise in the pulse rate indicates a serious complication

The *blood pressure* seems to be at its lowest at about the fourth or fifth day. During convalescence the blood pressure rises slowly to its normal, but may take a week or two to attain it Much of the feeling of depression and lassitude after influenza is associated with a decreased blood pressure.

There are no significant changes in the appearance of the tongue.

Vomiting usually ceases during the first 48 hours in the absence of complications or the excessive use of stimulating expectorants or sulfonamides *Diarrhea,* often associated with vomiting, is common in the first 48 hours

Epistaxis tends to be recurrent rather than obstinate and usually is not a frequent symptom If it is excessive, light packing is all that is required. If anemia should be found, it is not from nosebleed *Hemoptysis* is present if pneumonia is present

No important changes are present in the urine. It is scanty in amount, highly colored, and contains a small amount of albumin

DIAGNOSIS In the sporadic instances of the disease the diagnosis is purely clinical, supported by no other evidence The clinical features are considered to be sudden onset of fever, muscular aching, prostration and various signs of inflammation of the respiratory tract High morbidity rates, wide geographic extent, and a sharp increase in mortality from pneumonia characterize epidemics, many of which during the past century have been recognized on the basis of these criteria It is difficult to differentiate the clinical and epidemiologic characteristics of influenza from those of various other forms of respiratory disease.

Laboratory methods of diagnosis reveal that the different influenza viruses may produce a rather characteristic form of the disease, according to the foregoing criteria, as well as numerous mild atypical illnesses and obscure infections.

Hyperpnea and cyanosis are present. High fever is common in all severe cases. Rose spots occasionally appear from the seventh to the thirteenth day Leukocytosis, when it occurs, is considered to be due to secondary pneumonia from other organisms.

A clinical diagnosis is always presumptive. The presence of an atypical pneumonia or protracted fever in a patient who has a history of association with sick parrots or canaries justifies a suspicion of psittacosis Once it is suspected that the lung disease is psittacotic, a history of association with birds may be obtained. The bird is often the canary. The virus then can often be isolated by inoculation of citrated blood or sputum into mice.

The demonstration of complement-fixing antibodies is often employed to establish that a given acute illness is caused by a member of the psittacosis-lymphogranuloma group Complement-fixing antibodies may appear in the serum from 4 to 8 days after the onset of symptoms Additional serum specimens then are examined from time to time to ascertain a rise in titer within the next 4 or 5 days If there should be rise in the titer, it is significant. A serum titer of 1 16 or greater is suggestive of psittacosis if the serologic reaction for syphilis is negative and if there is no evidence of infection by the virus of lymphopathia venereum.

The mortality rate is about 1 in every 5 of those who have the disease.

DISEASES OF THE LUNGS DUE TO HIGHER ANIMAL PARASITES

The selective affinity of parasites for special tissues determines to a large extent the distribution of the lesions.

There are several parasitic worms that pass through the lungs during larval development and cause pulmonary disease, for instance, *Ascaris, Strongyloides,* hookworm, *Trichinella spiralis,* and *Echinococcus granulosus* The pulmonary invasion by *Trichinella spiralis* and *Echinococcus granulosus* may leave larvae in the lungs which may cause disease at a later date

Paragonimiasis. A parasitic trematode worm, or fluke, *Paragonimus westermani,* selects the lung as the preferred tissue of the host in which to reside, and causes the disease known as paragonimiasis.

Paragonimus westermani has a wide geographic distribution in the Orient and in South America The adult parasite has been found in mammals in Minnesota, Wisconsin, Michigan, Ohio, Mississippi, Kentucky, South Carolina and northern Canada, and in addition the larval forms have been observed in crayfish in Illinois, Indiana, Iowa, Louisiana, Missouri, Pennsylvania, Virginia, West Virginia and Ontario, Canada. Human infestation in North America, however, is rarely present

Man is infected by eating the raw or improperly cooked flesh of these crustacean hosts

The chief habitat of the adult parasite is the lungs The worms are enclosed in cystic cavities, which rupture into the bronchi, thereby permitting the ova to reach the sputum Externally the lungs show little change except scattered areas of congestion, emphysematous edges, and an uneven surface with reddish brown, superficial nodules In man these nodules usually number fewer than twenty and do not as a rule project from the surface These nodules are composed of cysts

Paragonimiasis is a slowly progressing chronic condition of insidious onset, resembling in many respects tuberculosis. Four types have been described· (1) general, (2) pulmonary, (3) abdominal and (4) cerebral

The general type is manifested by fever, enlargement of the superficial lymph nodes, especially the axillary and inguinal, with occasional cutaneous ulceration, and in cases of fatal infection, muscular rheumatic pains

In the predominating pulmonary type the patients have a chronic cough, most pronounced on rising in the morning, an abundant, blood-stained, rusty brown, purulent, tenacious sputum; and occasional attacks of hemoptysis, usually slight

tend to increase during the first few days of illness but may not reach the maximum until the eighth to the twelfth day. Rarely are there dyspnea and cyanosis.

Examination. On examination there may be a slight impairment of resonance on percussion if the lesion presents at the lung base. If the process is central, if it presents toward the axillae, or is in the upper pulmonary fields, percussion changes may not be found. Rales may be heard. Physical signs may become detectable only after the acute illness has passed Resolution of the pneumonia is often delayed for weeks This is the so-called nontubercular basilar infection of former days

In patients who present no objective physical findings the cold agglutination reaction has been found to be of some value in the diagnosis of this disease. The cold agglutination reaction is based on the presence of agglutinins which cause clumping of homologous or group O red cells at low temperatures. The test is not *infallible, since not all patients yield a positive reaction* *Furthermore, cold agglutinins* have been reported in paroxysmal hemoglobinuria, trypanosomiasis, pernicious anemia, leukemia, lymphoblastoma, cirrhosis, venous thrombosis and gangrene among others.

The leukocyte count is normal, or there may be a leukopenia. Leukocytosis if present may appear after several days. The sputum does not contain predominating bacteria Cold agglutinins appear during the second week in a majority of cases of primary atypical pneumonia and therefore are of no great diagnostic assistance

Diagnosis On general examination there may not be any pulmonary signs. Roentgenologic examination may present the first evidence of pulmonary involvement The lesion seems to begin at the hilus of the lung and spreads outward. However, in some instances roentgenologic examination does not reveal changes in the lungs during the active course of the disease. The disease is revealed after the symptoms have subsided.

In young adults the prognosis is good In older patients, whom the disease affects like bronchopneumonia, the outcome is more likely to be fatal

There is no effective treatment. Chemotherapy and antibiotic therapy are worthless or harmful

Psittacosis and Ornithosis (Psittacosis-Lymphopathia Viruses) The infective agents of psittacosis of birds and man, lymphopathia venereum of man, and murine and feline pneumonitis seem to be disease agents intermediate between the rickettsias and viruses. These belong to the so-called chlamydozoa and are gram negative organisms.

Psittacosis. Synonyms for psittacosis are ornithosis, parrot fever, psittacose, and Papageienkrankheit The avian psittacosis is caused by an elementary-body virus which develops in reticuloendothelial cells It is communicable to man.

Psittacosis is an acute and sometimes protracted febrile illness, with pulmonary lesions, which is transmitted from sick parrots to man A viral disease with similar pathologic manifestations is found in wild birds and tamed canaries, as well as in pigeons and chickens

The disease is severe, has a high mortality rate, and affects all ages and both sexes The incubation period is usually about 10 days, in exceptional cases as short as 4 or as long as 16 days

The pathologic changes observed are those of septicemia with localizing pulmonary lesions.

[illegible] There are general- [illegible] chills and rigors are [illegible] nty, mucoid, sometimes purulent, occasionally blood stained but infrequently rust colored. Abdominal pain, nausea and vomiting are common.

On examination after the fifth day of illness a few crepitant rales are present in the lungs. Later signs indicate patchy regions of consolidation in one or both lungs

the tissues become cyanotic, and peripheral edema appears. All of these changes are indicative of chronic passive congestion.

It may be inferred from the causes which originate chronic passive congestion of the lungs that essentially this process is one of chronic edema. An acute pulmonary edema may arise during the course of such a chronic passive congestion, and the latter constitutes one of the common causes of acute pulmonary edema.

Acute Pulmonary Edema. This is a serious condition which may be the immediate cause of death in cardiac and circulatory failures such as acute and chronic failure of the left ventricle, acute coronary thrombosis, angioneurotic edema, and the excessive intravenous administration of fluids Acute pulmonary edema may arise from extensive acute pulmonary disease such as pneumonia, extensive malignant metastasis, and inflammation produced by the inhalation of irritant gases.

The symptoms are the manifestations of lungs filled with fluid, with all of the anxieties and apprehensions of an individual drowning Add to this the agony of pain such as is present in the case of cardiac infarction and there is truly the combined picture of horror and death

On examination there is profound cyanosis of the face and extremities. The superficial veins of the face, neck and upper extremities are distended. The extremities are often dark and cold Pressure applied to the skin of such an extremity leaves a blanched area which remains white for some time

The vibrations from the audible rhonchi and rales are palpable. On percussion the note is flat over the posterior portions of the lower lobes There are so many noises present in the lungs that auscultation is not helpful diagnostically.

The diagnosis is usually obvious from inspection The roentgenoscopic examination often gives some clue to the physical state of the heart, lungs, pleura and mediastinum.

Pulmonary Embolism. Embolism is the sudden obstruction of the lumen of a blood vessel by a blood clot, air, fat or any other substance which has been brought to its place by the blood current.

The commonest embolus reaching the larger pulmonary arteries is composed of clotted blood. Such blood clots may arise in the heart affected by valvular heart disease, or in the larger veins, usually those of the legs. In the leg veins there are two conditions prone to create emboli These conditions are phlebothrombosis and phlebitis. In phlebothrombosis there is no evidence of antecedent disease or injury of the vein. Thrombosis is first. The phlebitis develops as a reaction to the thrombosis

Embolism, usually in the lungs, is the most serious complication of postoperative venous thrombosis. It is often the result of phlebothrombosis and occurs in many cases in which there is no clinical evidence of thrombophlebitis Therefore it is assumed that thrombosis has occurred in some one of the peripheral veins and that either the entire thrombus became the embolus, or the part of it which remained at the original site failed to produce local symptoms.

Surgical exploration for inoperable carcinoma associated with metastasis is accompanied with high incidence of postoperative pulmonary embolism. Usually the magnitude of the surgical procedure is directly related to the frequency of embolism, which is twice as common after repair of bilateral hernia as after operations for unilateral hernia

When pulmonary embolism occurs after the clinical manifestations of thrombophlebitis have appeared, the emboli are likely to be small and nonfatal. It is commoner to observe phenomena of pulmonary embolism a few days before clinical thrombophlebitis than after the symptoms of thrombophlebitis have appeared.

though at times severe. The physical signs may suggest lobular pneumonia or tuberculosis.

A definite diagnosis is established by finding the ova in the sputum, the feces or in the cutaneous or subcutaneous tissues of a patient who has pulmonary disease.

In light infections prognosis is good, although spontaneous cure may not occur. *In heavy invasions*, superimposed tuberculosis, secondary pyogenic infections, or cerebral involvement the prognosis is unfavorable.

Echinococcus Cysts of the Lungs. Echinococcus cysts of the lungs are caused by *Echinococcus granulosus*, of the superfamily Taenioidae.

The symptoms, if any are present, are cough, hemoptysis, dyspnea and pain. The cough is dry and hacking and may be accompanied by slight mucoid expectoration Hemoptysis in small quantities may occur. Mild thoracic discomforts, but rarely pain unless the pleura is reached, may develop, as may a pleural rub also. In pleural involvement there may be a low-grade fever The cyst may give pressure symptoms which are followed by rupture into a bronchus, or it may penetrate the pericardium, a chamber of the heart, the vena cava or the thoracic wall

The rupture of a cyst into the bronchial tree originates sudden distress, pain and the expectoration of quantities of thin, blood-stained fluid If the patient survives the rupture, the diagnosis of hydatid cyst becomes evident as fragments of cyst are coughed up After rupture, urticaria is common. Sudden death has followed the impaction of fragments of the cyst in the glottis. Profuse hemoptysis may occur at the time of rupture or later and may prove fatal

On examination over the cyst fremitus is diminished or absent. Percussion dullness may be elicited There is often displacement of mediastinal structures Auscultation may reveal changes in respiratory sounds because of the space-occupying cyst Crackling or musical rales are common Occasionally percussion and auscultation may be altered by the effects of a bronchial communication. Roentgenologic examination reveals the cysts

The diagnosis is made by identification of the parasite or the cysts The intradermal and the complement fixation tests may be helpful The clinical manifestations and the roentgenologic evidence are often diagnostic Puncturing and aspiration of the cysts are contraindicated because of the danger of rupture and anaphylactic phenomena. If the situation of the cyst is favorable for surgical approach, operation should be considered

DISEASES OF THE LUNGS SECONDARY TO CIRCULATORY DISTURBANCES

Acute and Chronic Pulmonary Congestion. Acute and chronic pulmonary congestion occurs in certain primary and secondary diseases of the lungs The primary diseases of the lungs which are characterized by acute congestion are the acute infections and the acute injuries from physical and chemical agents. Acute congestion from primary disease of the lungs may be localized, as in the pneumococcal pneumonias, or generalized when provoked by the inhalation of an irritating gas

Chronic congestion of the lungs occurs less frequently from primary pulmonary disease than it does from disease in which the lungs are secondarily congested, as in heart failure from disease of the mitral valves. Chronic passive congestion of the lungs, as it occurs in mitral heart disease, renders the lungs less elastic and more rigid than normal. The lining of the bronchial tubes is malnourished and desquamates and thus permits fluid and erythrocytes to exude from the capillaries into the air passages to be expectorated. Cough and increased expectoration may be the only complaint that a patient has for seeking help However, before long the patient has dyspnea and the sputum becomes reddish brown (rusty) in color, the peripheral veins are dilated, the capillaries are widened and pulsate, the skin of the lips and

the tissues become cyanotic, and peripheral edema appears. All of these changes are indicative of chronic passive congestion.

It may be inferred from the causes which originate chronic passive congestion of the lungs that essentially this process is one of chronic edema. An acute pulmonary edema may arise during the course of such a chronic passive congestion, and the latter constitutes one of the common causes of acute pulmonary edema.

Acute Pulmonary Edema. This is a serious condition which may be the immediate cause of death in cardiac and circulatory failures such as acute and chronic failure of the left ventricle, acute coronary thrombosis, angioneurotic edema, and the excessive intravenous administration of fluids Acute pulmonary edema may arise from extensive acute pulmonary disease such as pneumonia, extensive malignant metastasis, and inflammation produced by the inhalation of irritant gases

The symptoms are the manifestations of lungs filled with fluid, with all of the anxieties and apprehensions of an individual drowning Add to this the agony of pain such as is present in the case of cardiac infarction and there is truly the combined picture of horror and death

On examination there is profound cyanosis of the face and extremities. The superficial veins of the face, neck and upper extremities are distended. The extremities are often dark and cold Pressure applied to the skin of such an extremity leaves a blanched area which remains white for some time.

The vibrations from the audible rhonchi and rales are palpable. On percussion the note is flat over the posterior portions of the lower lobes. There are so many noises present in the lungs that auscultation is not helpful diagnostically.

The diagnosis is usually obvious from inspection. The roentgenoscopic examination often gives some clue to the physical state of the heart, lungs, pleura and mediastinum.

Pulmonary Embolism. Embolism is the sudden obstruction of the lumen of a blood vessel by a blood clot, air, fat or any other substance which has been brought to its place by the blood current

The commonest embolus reaching the larger pulmonary arteries is composed of clotted blood Such blood clots may arise in the heart affected by valvular heart disease, or in the larger veins, usually those of the legs In the leg veins there are two conditions prone to create emboli These conditions are phlebothrombosis and phlebitis In phlebothrombosis there is no evidence of antecedent disease or injury of the vein Thrombosis is first. The phlebitis develops as a reaction to the thrombosis

Embolism, usually in the lungs, is the most serious complication of postoperative venous thrombosis It is often the result of phlebothrombosis and occurs in many cases in which there is no clinical evidence of thrombophlebitis Therefore it is assumed that thrombosis has occurred in some one of the peripheral veins and that either the entire thrombus became the embolus, or the part of it which remained at the original site failed to produce local symptoms.

Surgical exploration for inoperable carcinoma associated with metastasis is accompanied with high incidence of postoperative pulmonary embolism Usually the magnitude of the surgical procedure is directly related to the frequency of embolism, which is twice as common after repair of bilateral hernia as after operations for unilateral hernia

Thrombophlebitis predisposes to pulmonary embolism, but there are reasons for believing that the clinical manifestations of peripheral thrombophlebitis are associated with fixation of the thrombus by inflammation.

When pulmonary embolism occurs after the clinical manifestations of thrombophlebitis have appeared, the emboli are likely to be small and nonfatal. It is commoner to observe phenomena of pulmonary embolism a few days before clinical thrombophlebitis than after the symptoms of thrombophlebitis have appeared

Allen, Barker and Hines have stated that when a patient has a pulmonary embolism after operation and survives, there is a 43 8 per cent chance of another thrombotic episode, a 30.5 per cent chance of another embolism and an 18.3 per cent chance of a fatal embolism in the same postoperative convalescence. The incidence is less in cases of thrombophlebitis than in cases of phlebothrombosis but is still definitely higher than in all postoperative cases as a group

Pulmonary embolism affects men much more frequently than women, despite the preponderance of operations on the lower part of the abdomen among women.

SYMPTOMS. The symptoms depend on the amount of lung tissue which is incapacitated by the occluded artery. The occlusion of a small pulmonary artery may occur without noticeable symptoms. The occlusion of a relatively large pulmonary artery produces cor pulmonale and shock. The occlusion of a large or several small pulmonary arteries may be immediately fatal

On occasion the patient who has a pulmonary embolism will have a sudden feeling of apprehension, anxiety, palpitation and dyspnea. These symptoms are often so severe that the patient is fearful of moving. The duration of the attack is often from 15 to 30 minutes Several hours or a day or two elapse before pleuritic pain or hemoptysis occurs.

Pleuritic pain which occurs in about one week to 10 days after an operation is often caused by pulmonary embolism. A distinctive feature of pulmonary embolism often is dyspnea out of proportion to restriction of respiratory movements and associated pain The pain occurs as the result of the embolus reaching a peripheral pulmonary artery and thus involving the pleura Despite pain a small embolus gives no general symptoms, and the patient maintains a sense of well-being

Hemoptysis occurring after operation should be regarded as evidence of pulmonary embolism The patient coughs up small blood clots or expectorates a thick, bloody sputum As time passes, the coughed-up blood becomes darker and decreases in amount

Small pulmonary emboli with minimal or no symptoms often occur. This occurrence indicates that the patient is susceptible to thrombosis and resultant embolism. Once this process is initiated, it will recur often and there is danger of subsequent massive pulmonary embolism

In *massive pulmonary embolism* there is an initial shock. The initial shock of a large pulmonary embolus may be survived and if so a prolonged febrile illness may follow The illness results from a large pulmonary infarct which may or may not break down to produce pulmonary abscess. This condition resembles pneumonia and is difficult to differentiate from pneumonia

EXAMINATION. The findings on physical examination after pulmonary embolism are exceedingly variable and often inconclusive. Rales, percussion dullness and pleuritic friction sounds are irregularly present in the beginning As time passes the physical signs of a localized pneumonia may appear. The presence of unilateral pleural effusion after a surgical operation is highly suggestive that pulmonary embolism has occurred

Examination soon after a large pulmonary embolus has occurred reveals evidence of shock In smaller but definitely manifested emboli there are present dyspnea, perhaps orthopnea, and always varying degrees of apprehension If a large area of the lung has been embolized there is an increased pulsation in the second and third interspaces to the left of the sternum and a loud systolic murmur with accentuation of the second pulmonic sound Gallop rhythm is present occasionally. The veins of the neck are dilated and pulsating. There is an initial fall of temperature and then a rise to 101 or 103 F (38.3 or 39 4 C) as the evident degree of shock abates. There may be scattered or numerous moist rales in the lungs, and the breath sounds may be distant or suppressed over the affected portion of the

lung. Signs of the local accumulation of fluid in the pleural space may develop after a few days. Rather severe and persistent hemoptysis often is evident.

There is no characteristic roentgenographic evidence of a large pulmonary infarct. Large infarcts frequently produce elevation of the diaphragm on the affected side, indefinite thickening of the pleural shadow in the costophrenic angle and occasionally the appearance of a small amount of pleural fluid

Electrocardiographic changes which are indicative of acute cor pulmonale occurring with severe pulmonary embolism may be present The changes in the electrocardiogram may develop at any time during the first 48 hours after the embolism occurs, and they may be transient, but when they are found they are significant (Barnes).

A large pulmonary embolus is one of the causes of sudden death. Some patients may live for a few minutes after the episode or, more rarely, a few hours may elapse before death occurs.

Diagnosis. The occurrence of sudden pleural pain from 6 to 21 days after an operation, obstetric delivery or severe injury should be regarded with great suspicion since other conditions causing pleurisy are rare in those periods Sudden death occurring in the same group of patients during the same interval should be considered as most likely the result of a large pulmonary embolus, particularly if the clinical course has otherwise been normal If pleural pain, hemoptysis and shock, as produced by a relatively large pulmonary embolus, occur in a patient who has acute or recent thrombophlebitis, the diagnosis of embolism can almost certainly be made, but as has been stated, most embolisms occur before thrombophlebitis is clinically evident.

The one condition difficult at times to differentiate is an acute coronary thrombosis. The electrocardiogram is of great value in distinguishing acute coronary thrombosis from pulmonary embolism since the patterns are different even if the coronary thrombus is in the posterior descending branch. In coronary thrombosis frequently the pain is more severe, it is not pleural, it often extends to the arms or shoulders, cyanosis is infrequent, and signs of a localized pulmonary lesion are absent.

The electrocardiographic changes in infarction of the posterior ventricular wall and those present in pulmonary embolism are somewhat similar The deep S and the inversion of the T waves present after pulmonary embolism do not occur in infarctions of the posterior ventricular wall.

The signs and symptoms of small pulmonary infarcts usually disappear within a week with the possible exception of some residual elevation of the diaphragm on the affected side.

Air Embolism. Air embolism may occur in two forms (1) pulmonary venous air embolism and (2) arterial air embolism

In the pulmonary form, air enters one of the systemic veins and is carried to the right side of the heart and pulmonary circulation and depends for its effects on mechanical obstruction of the outflow channel of the right ventricle.

In arterial embolism the air gains entrance to the pulmonary venous channels and is propelled from the left ventricle to those systemic arteries which supply the superiorly located portions of the body Since a small amount of air can effectively block a medium-sized artery, serious consequences may result when a few milliliters of air enter the pulmonary vein and are carried into either the coronary or cerebral circulation or both

In the pulmonary form the presence of air in the right ventricle produces a loud, churning sound, often readily heard without stethoscopic aid, which is known as the millwheel murmur This murmur appears almost immediately after air has entered the venous circulation

expectoration are absent except when conditions such as bronchial infections or asthma are present Cyanosis and compensatory polycythemia may appear

EXAMINATION. Inspection in severe emphysema reveals the thorax permanently in the position of deep inspiration with slight movements of the thoracic wall; the phrenic wave sign is absent The lungs have lost their elastic recoil so that the intercostal and abdominal muscles are used for breathing. Owing to the voluminous lungs the diaphragm is stretched and its function is impaired Therefore the neck and *intercostal muscles* may actively support inspiration. The action of the latter muscles pulls the thoracic wall upward and forward. The expanded lungs extend into the pleural sinuses and between the heart and thoracic wall, resulting in increase of the anteroposterior diameter of the thorax and dorsal kyphosis.

If the emphysema is severe, cyanosis may be observed and the veins of the neck are distended In some cases there is clubbing of the fingers and toes.

On palpation decreased expansion of the thoracic wall and diminished tactile fremitus are evident The percussion note is hyperresonant and the lower margins of the lungs extend below their normal limits. The area of cardiac dullness is diminished and the liver is in a low position On auscultation the expiratory phase of respiration is prolonged and low-pitched Whispered voice sounds are diminished Rales are elicited only when other conditions such as asthma and bronchitis are present

DIAGNOSIS The appearance of the patient, in combination with the physical and roentgenologic findings, is diagnostic.

Many persons endure emphysema over long periods of time.

Senile Emphysema. Elderly persons who have kyphosis of the thoracic vertebrae and some who do not have deformities of the spinal column may have a general narrowing of the thorax and the intercostal spaces and a decrease in the respiratory movements of the thoracic wall without symptoms

On examination, tactile fremitus is diminished, the percussion note is hyperresonant, and auscultation reveals diminished breath sounds. Often only the expiratory phase of respiration is heard

The diagnosis is made during routine physical examinations.

Traumatic or Interstitial Emphysema. Rupture of alveolar walls may result from needle puncture, crushing or tearing injuries of the chest, violent coughing, and from the use of a pulmotor Interstitial emphysema may develop in those who are enjoying health without evidence of disease (spontaneous interstitial emphysema)

The escaped air from the lung may spread through the interstitial tissue and through the hilus and thence into the mediastinum (*mediastinal emphysema*); thence it may spread into the tissues of the neck and occasionally gives rise to generalized, subcutaneous emphysema

SYMPTOMS. When the amount of air is small, there are no symptoms When a large amount of air escapes, some of it may dissect along the connective tissue bands surrounding the blood vessels and form blebs on the pleura. When a bleb ruptures, spontaneous pneumothorax occurs.

In some instances the first symptom is severe pain beneath the sternum or in the side of the thorax The pain may extend to the left side of the neck and down the left arm. The pain of spontaneous interstitial emphysema disappears soon after the attack

EXAMINATION. The late Louis Hamman described, as being characteristic of this condition, a peculiar crackling, crunching sound heard over the sternum and precordium which is synchronous with the heart beat This sound may be heard with *the patient* in any position, but it is more likely to be elicited when the patient lies on the left side or leans forward. These sounds convey the impression of air being churned or squeezed in the tissues. Often they are so loud that they can be heard by the patient. Interstitial emphysema causes a hyperresonant note to percussion over

the usual region of cardiac dullness. In some cases signs of spontaneous pneumothorax occur.

DIAGNOSIS. The history and the examination by physical means are diagnostic. The results of roentgenologic examination are negative unless pneumothorax is present

Symptoms soon disappear.

TUMORS OF THE LUNG

Tumors of the lung may be arranged in certain groups based partly on the manner of origin and partly on the tissue from which the tumor originates (1) Bronchial malformations may be productive of benign cystic and papillary structures. The congenital cystic malformations are of two types. (a) overgrowth of misplaced fetal portions of the bronchial tree and (b) overgrowth of areas of fetal bronchiectasis resulting from inflammation and leading to occlusion of a bronchus and retention of mucus (2) Mixed tumors, also of fetal origin, arise from fetal pulmonary tissues which fail to develop into normal pulmonary structures These tumors may be designated as chondromas or sarcomas. When the epithelial elements predominate they are termed adenoma, alveolar carcinoma or adenocarcinoma. Hamartoma of the lung may contain cartilage and is thus related to the chondromas. However, not all hamartomas contain cartilage. (3) The myxomas and fibromas of the periphery of the lung probably arise from the pleura. (4) The solid diffuse carcinomas which arise as a sequel or incident to inflammations such as a chronic tuberculous pneumonia are difficult to separate from bronchial carcinoma.

Regardless of the origin of lung tumors which may be classified as being benign tumors, they are comparatively rare The so-called bronchial adenoma and the chondroma or hamartoma are the commonest benign tumors of the lung.

The detection of these lung tumors is accomplished by roentgenologic examination The diagnosis awaits histologic study The prognosis, of course, depends on the degree of anaplasia of the cells

Metastatic Malignant Disease of the Lung. Metastatic malignant lesions of the lungs are many times more frequent than primary ones

Epithelial Malignant Lesions. Carcinomas, hypernephromas and chorionepitheliomas almost always give secondary pulmonary involvement. Carcinomas of the breast frequently metastasize to the lungs Malignant lesions of the thyroid gland, air passages, alimentary tract and its associated glands, the urinary organs, genitalia and extremities often aid in the destruction of the patient through metastasis to the lungs.

Pulmonary metastasis occurs by (1) direct extension, (2) blood stream implantation and (3) lymphatic spread The metastatic lesions usually involve the lower portions of the lungs They appear as (1) single or multiple nodular growths in one or both lungs and (2) infiltrative or diffuse growths in both lungs. A lung is more completely filled with secondary malignant disease in instances of extension from cancer of the breast than in extension from cancer elsewhere The affected lung usually corresponds to the breast involved by carcinoma The pleura is often extensively involved, as shown by a hemorrhagic or serofibrinous effusion

SYMPTOMS A few who have metastatic pulmonary carcinoma may have cough, vague thoracic discomforts and at times pleuritic pain Dyspnea may be a distressing symptom and hemoptysis is common However, on roentgenologic examination the lungs are frequently found to be involved without there having been any symptoms or findings on examination of the thorax by physical means.

EXAMINATION. In early periods of metastatic pulmonary tumors there may be observed a suppression of the breath sounds, especially pronounced during inspiration and sometimes accompanied by fine crackling rales over a limited area of the thorax. As the tumor or tumors grow, decreased expansion ensues The percussion

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note then becomes flat, and bronchovesicular or bronchial breathing and sibilant and sonorous rales are present. Signs of pleural effusion may be found early or at least during the course of the disease. These signs are usually manifest over the lower half of the lungs particularly.

DIAGNOSIS. Roentgenologic examination is usually diagnostically conclusive It is well to try to confirm the diagnosis, if possible, by repeated cytologic examinations of the sputum. Bronchoscopy is of little or of no diagnostic value.

Sarcomas. Metastatic involvement of the lungs by sarcomatous tumors is proportionately commoner than by carcinomatous tumors Sarcomas arising in almost any part of the body metastasize and secondarily involve the lungs

SYMPTOMS In metastatic pulmonary sarcoma, as in other pulmonary malignant diseases, both primary and secondary, cough, pain in the thorax, dyspnea and hemoptysis are the usual symptoms

EXAMINATION. When metastatic nodules have attained considerable size in the lungs, dullness or flatness to percussion is elicited. Sibilant and sonorous or musical rales are heard, and the breath sounds are decreased and changed to a bronchial tone. Massive growths obliterate all resonance, breath sounds and vocal fremitus or transmission of voice sounds over an entire lung field or over most of the thorax, even in the absence of sufficient fluid to produce such signs. In some cases bulging or retraction of the thorax or the intercostal spaces may be visible.

DIAGNOSIS The presence of metastatic pulmonary malignant disease in a patient known to have a sarcomatous tumor in any part of the body is assumed to be pulmonary sarcoma unless proved to be otherwise. The physical signs and the roentgenoscopic findings are diagnostic of a malignant tumor of the lung only, not of the type of tumor

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10

DISORDERS OF THE HEART, BLOOD PRESSURE, PULMONARY ARTERIES AND THORACIC AORTA

THE HEART

The average adult heart measures about 5 inches (12 7 cm.) in length, 3 inches (7.6 cm.) in width, and 2½ inches (6 4 cm) in thickness The average weight of the healthy adult heart of a man is about 9 ounces (280 gm) and of a woman, 8 ounces (250 gm) These weights may be doubled in instances of cardiac enlargement.

Outlines of the Heart. The base or upper margin of the heart, from which the great vessels go off, lies in the second intercostal space or at the upper margin of the third rib behind the sternum It is here that the superior vena cava ends and the aorta begins. The base of the heart extends from about ½ inch (1 3 cm.) to the right of the sternum to about 1 inch (2 5 cm) to the left of the sternum.

The *right margin* of the heart, formed by the right atrium, lies from about 1½ to 1¾ inches (3.8 to 4 5 cm) to the right of the median line, at the upper border of the third costal cartilage, and extends in an outwardly curved line to the junction of the seventh rib and the sternum In the fourth interspace it may reach 1 inch (2 5 cm) beyond the right edge of the sternum

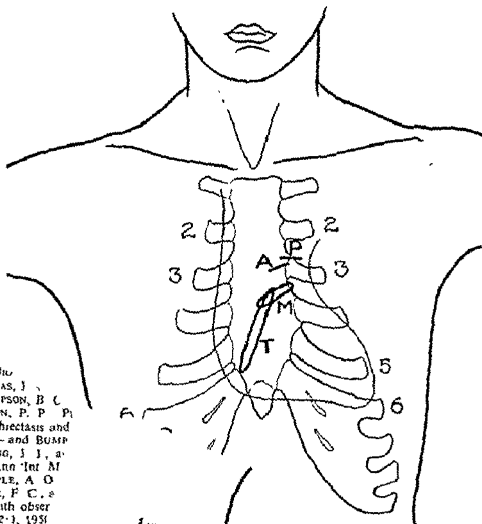
The *left margin* of the heart passes somewhat obliquely downward, from 1 inch (2.5 cm) to the left of the sternum at the upper border of the third costal cartilage, and to the left to the region of the apex

The curved sternocostal surface of the heart, which proceeds upward and forward and comes into direct contact with the anterior wall of the thorax, is formed chiefly by the right atrium and the right ventricle, it lies just behind the sternum and behind the anterior extremities of the third, fourth, fifth and sixth ribs, being in part overlapped by the margins of the lungs

The *lower margin* of the heart passes from the seventh right chondrosternal junction across the sternoxiphoid joint outward in the fifth interspace to the apex beat, which is from 1⅗ to 2 inches (4 1 to 5 1 cm.) below and to the inner side of the nipple and about 3½ inches (8.9 cm) to the left of the median line. This marks the extreme left limit of the heart. In children the apex is higher in the fourth interspace In old people it is lower

The diaphragmatic surface of the heart, posterior and inferior, is almost flat where it is in contact with the diaphragm The left atrium lies at the back of the heart and is directed toward the esophagus and spinal column, the left ventricle lies behind and below, only a small portion of it projecting forward to form the apex of the heart The auricle of the left atrium is in contact with the anterior wall of the thorax close to the pulmonary artery The orifice of the pulmonary artery is situated at the sternal end of the third left intercostal space; the orifice of the aorta lies just below the middle of the left half of the sternum at the same level The center of the mitral orifice lies behind the third left intercostal space close to the sternum, and the center of the tricuspid orifice lies behind the right half of the sternum at the level of the sternal end of the fourth intercostal space (Fig 10-1).

The atrioventricular (auriculoventricular) groove or line of junction between the atria (auricles) and ventricles runs from the sixth right chondrosternal junction upward and to the *left* to the *third* left chondrosternal junction. The atria lie above and to the right of this line, and the ventricles below and to the left.



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Fig. Topographic location of the valves. P, pulmonic valve. T, tricuspid valve. M, mitral

The right atrium (auricle) and right ventri... the left atrium and left ventricle lie posteriorly. In the right atr... runs the right coronary artery. Because it lies on the anterior ... heart it is likely to be injured in stab wounds and thus give rise to ... as may also the interventricular branch of the left coronary artery, w... near the left border of the heart between the right and left ventric... The position and size of the heart may be determine...

of examination: (1) the inspection and palpation of the apex beat of the heart, (2) the percussion of the cardiac dullness, and (3) the delimitation of the margins of the heart by means of roentgenologic examination.

POSITION OF THE APEX BEAT OF THE HEART. In the healthy and not too fat man an elevation of the thoracic wall, at regular intervals, at the times of the systoles of the left ventricle, can be seen and felt in the left fifth intercostal space between the mammillary and the parasternal lines. When the heart is enlarged, the apex beat changes its position; it may occupy the sixth, seventh or eighth interspace instead of the fifth, and may be as far as 2 or 3 inches (5.1 to 7 6 cm.) to the left of the nipple line.

The site of the apex beat is the most lateral and the lowest part of the area of pulsation. The apex beat thus recorded, according to H. L Smith, does actually correspond to the position of the heart's apex. Thus the point of maximal impulse (p m i.) is almost always at the site of the apex beat

The position of the apex beat with the patient standing is practically the same as in the recumbent position On deep inspiration, the apex beat may descend and lie behind the sixth rib or in the sixth intercostal space; on deep expiration, in the young and healthy person, it may rise as high as the fourth intercostal space and become more diffuse. The position changes when the patient lies on his left side; it may then reach the mammillary line or, often, a point to the left of it. After rapid emaciation this mobility may be greater, when the patient lies on his right side, the apex is very little displaced to the right, rarely passing to the right of the left parasternal line.

The position of the apex beat varies somewhat with the shape of the thorax in the different somatic types and as the results of thoracic deformities. Anything that lowers the diaphragm lowers the apex beat also, anything that raises the level of the diaphragm (meteorism, ascites, pregnancy, abdominal tumors) will raise the position of the apex beat. Fluid or air in one pleural cavity will displace the apex beat toward the opposite side; retraction of a lung may have an opposite effect Enlargement of the left ventricle displaces the apex downward and to the left, enlargement of the right ventricle displaces the apex to the left but not downward A pericardial effusion may displace the apex beat upward to the third intercostal space.

Too much stress should not be laid on slight abnormalities in the position of the apex beat. Its determination, however, is the first step in the attempt to ascertain the position and size of the heart, inasmuch as the position of the apex indicates the situation of the left margin of the heart.

Precordial boss and voussure are the names given to a unilateral bulging occupying the precordial area in children This bulging is due to enlargement of the heart or to pericardial effusion The enlargement is oval, its long diameter being vertical and extending from the third to the sixth rib near the sternum It can arise only in early life while the ribs are still flexible.

PERCUSSION OF AREAS OF CARDIAC DULLNESS By percussion on the anterior surface of the thorax, the area of cardiac dullness often can be outlined, particularly in young and healthy persons Two areas of cardiac dullness may be delineated These areas are (1) that of the superficial, small cardiac dullness, and (2) that of the deep, or relative, cardiac dullness The area of small dullness corresponds to the part of the sternocostal surface of the heart not covered by the lungs, while the [illegible]
The [illegible]
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this area the characteristic resonant pulmonary note is absent. The larger area of relative dullness is outlined by percussing from the lungs toward the heart and marking the points at which the percussion note becomes less resonant or relatively

dull. Though the heart is covered by the lungs at its periphery, the change in the percussion sound elicited after practice and experience permits the determination of approximate outlines of the heart with reasonable accuracy. The determination of the superficial dullness is much easier than determination of the deep dullness; for the latter a degree of skill, obtainable only by considerable practice, is required

In obesity and in emphysema the determination of the relative dullness is difficult if not impossible. The area obtained is much smaller than that corresponding to the true dimensions of the heart When the dullness passes to the right as far as the right parasternal line or farther, and upward as high as the second rib, while the left margin of the heart is as far as, or farther to the left than normal, it is certain that the heart is enlarged

Dilatation, principally of the left ventricle, causes an expansion of the area of dullness toward the left only. Dilatation of the right ventricle displaces the right margin of the area of relative dullness to the right. When both relative and absolute dullness are increased to the right of the sternal margin, there is usually either a dilatation of the right atrium or a pericardial exudate.

The apparent area of cardiac dullness as outlined by percussion may not be cardiac dullness at all but may result from the presence of tumors in the neighborhood, of pleural effusions, or of infiltrations of the lungs. Similarly, a dislocation of a heart of normal size by a pleural effusion, by a tumor, or by a pneumothorax may simulate an abnormal position of one cardiac boundary due to enlargement.

Diminution of the Area of Dullness. Seldom does this indicate diminution in size of the heart, often it is due to emphysema.

The percussion of the heart is a subjective method of measuring the heart which has much value, though the error is often considerable A high degree of accuracy in percussion is impossible for many reasons. There are no sharp margins of cardiac dullness to be obtained by percussion in the various intercostal spaces No outlines of the heart by percussion are as important diagnostically as the finding of a well-defined point of maximal impulse. The value, then, of percussion of the heart lies mainly in enabling confirmation of the suspected left limits of the heart when the impulse is ill-defined. This feat is often of enough value to reward for the time spent in the practice of percussion, and much time is required

Normal and Abnormal Sounds Over the Heart and Vessels Obtained on Auscultation. In health and in disease oscillations arise in the heart and blood vessels that may cause audible sounds. These can be recognized by listening with the naked ear or with the aid of the stethoscope

THE HEART SOUNDS If the ear or a stethoscope is placed over the thorax in the cardiac region of a healthy person, pairs of sounds are heard recurring at regular intervals Each pair of sounds consists of a first and a second sound, separated from each other by a brief interval Each pair of sounds in turn is separated from the next pair by a longer interval The duration and accentuation of the single sounds at the apex of the heart are found to be somewhat different from the duration and accentuation at the base; thus at the base and over the lower part of the sternum the first sound is longer and more accentuated, phonetically indicated as *lúbb-dupp*, whereas at the apex the second sound is more accentuated, the rhythm becoming that of *lubb-dúpp*. The first sound of each pair is synchronous with the apex beat of the heart. The second sound occurs at the very beginning of ventricular diastole. The long pause separating consecutive pairs is diastolic in time.

Origin of the Normal Heart Sounds. The origin of the *first sound* has been shown by H. L. Smith, Essex and Baldes to be chiefly due to closure of the mitral and tricuspid valv[illegible] is an element of intracardial tension tone due to oscillations [illegible] ions of the walls of the ventricles, it is less important in aus[illegible]

The *second sound* is coincident with and due to the closure and tension of the semilunar valves of the aorta and pulmonary artery at the beginning of diastole.

In children and young adults occasionally the trained ear may hear a *third sound*, audible just after the second sound It is said to be best heard at or near the apex when the patient is somewhat turned to the left side.

Auscultation Sites. The sites selected for auscultation are those at which the vibration of the particular valves in question is best heard. These auscultation sites for the pulmonary and tricuspid valves correspond to anatomic projections of the valves. The auscultation sites for the aortic and mitral valves do not correspond to the surface overlying the anatomic sites of these valves.

The four principal auscultation sites are (1) at the apex of the heart, for the mitral valves (mitral area); (2) at the second left intercostal space close to the sternum for the pulmonary semilunar valves (pulmonary area); (3) at the second right intercostal space close to the sternum for the aortic valves (aortic area); and (4) at the junction of the fifth rib with the sternum on both the right and left sides for the tricuspid valve (tricuspid area)

Rhythm and Accentuation At each auscultation site both sounds of the heart are audible, and experience and training teach the art of distinguishing, at each site, the sound of autochthonous origin from the propagated sound Thus over the pulmonary and aortic sites the second sounds are autochthonous and the first sounds are propagated.

Identification of the Heart Sounds. Over a healthy heart the distinguishing of the first sound from the second sound is readily accomplished by the accentuation and by the length of the pause following each sound In disease, however, the heart beats may become very irregular or the rate greatly accelerated Both the long pause and the first sound become relatively shortened and the heart sounds are like those of a fetus, so that the ear may not be able to distinguish the first from the second sound In such a case the examiner may help himself by palpating (simultaneously with auscultation) the apex beat or the carotid pulse.

The loudness of the sounds of the heart may be less or greater than normal.

Enfeeblement of the First Sound. The first sound is enfeebled when something exists that hinders the transmission of the sound, such as obesity, pulmonary emphysema, large pleural or pericardial effusion, defective contraction of the ventricles or alterations of the atrioventricular valves A feeble contraction of the ventricle may occur in any of the conditions that give rise to myocardial insufficiency. When vegetations appear, as in acute endocarditis, on the borders of the valves, the first sound may be diminished or may even disappear

Accentuation of the First Sound The first sound may be exaggerated in intensity when the transmission of the sound is facilitated, as in emaciated patients, or when there are gas-containing cavities near the heart (pneumopericardium, dilated stomach) Abrupt ventricular contraction, such as often occurs in emotional excitement or on physical exercise, augments the first sound, and certain alterations in the atrioventricular valves, such as thickening or induration, may have the same effect The latter may explain the loud first sound sometimes heard in chronic endocarditis, for example mitral insufficiency, and in arteriosclerosis of a mitral cusp

A marked accentuation of the first sound at the apex often indicates the existence of mitral stenosis The abrupt first sound heard in this disease is believed to be due to the more powerful vibrations set up by the sudden tension of the stiffened valve cusps

Enfeeblement of the Second Sound. The second sound may be feebler than normal owing to faulty transmission to the stethoscope, as in obesity, pulmonary emphysema, and pericardial effusion, and owing to lowering of tension in the aorta or pulmonary artery, as in myocardial insufficiency, anemia, hypotension, and in general debility.

The lesion of mitral insufficiency tends to enfeeble the first sound When in the course of a mitral stenosis a mitral insufficiency develops, the first sound may become somewhat feebler.

Accentuation of the Second Sound. The second sound may be exaggerated (accentuated) whenever the arterial tension is increased. Thus, marked accentuation of the aortic second sound usually indicates hypertension in the aorta.

When in addition to accentuation of the aortic second sound there is alteration of the quality or timbre, there often are changes in the semilunar valves themselves, in which case the sound is loud and has a certain tympanitic or ringing quality.

When the accentuation of the second sound is maximal to the right of the sternum, it is certainly aortic in origin, but when it is maximal to the left of the sternum, it is usually pulmonary though it is sometimes due to a sound propagated from the aortic orifice.

The pulmonary second sound is accentuated normally during youth; otherwise it is evidence of abnormally increased pressure in the pulmonary artery and may be due to some obstruction to the flow of blood in the lungs, such as emphysema, fibroid phthisis, or pulmonary arteriosclerosis, or to faulty circulation in the left heart

Changes in the Number of the Heart Sounds. Instead of the first and second sounds of the heart, there may be heard, either in healthy or in diseased hearts, three or four or even more sounds. The additional sounds may be due (1) to failure of the components of the first or second sounds to fuse to a single sound, especially when there is a disturbance in the synchronism of events in the two ventricles, or (2) to the formation of new sounds

Splittings and Doublings of the Heart Sounds (¾ Rhythm) The first sound ... marked altera-

the fault in coincidence is greater. Similarly the second sound may be either split or doubled Every degree of transition from slight splitting to distinct doubling may be met with. These phenomena are frequently noted in health at different phases of respiration. The doublings are common too in disease conditions, and are then audible in all respiratory phases When the mitral valve is damaged, the second sound is often split at the base. A splitting of the second sound at the apex is common in mitral stenosis.

Triple or Gallop Rhythms (¾ Time). The normal rhythm of the heart is fairly well maintained in the splittings and doublings Sometimes the heart sounds, however, appear as groups of three sounds, of which the first and second and the second and third are separated by approximately equal intervals, while the last member of each group is separated from the first member of the next succeeding group by a somewhat longer pause, and for this reason it is fancied to resemble the sounds of the hoofs of a galloping horse (an awkward nag), three hoofs down followed by the fourth hoof (gallop rhythm)

The terms presystolic gallop and protodiastolic gallop are contradictory. These extra sounds are related to the complex of sounds constituting the first heart sound. They are neither diastolic nor systolic in time. Sometimes the extra sound precedes the first sound of the series (presystolic gallop), sometimes it follows (protodiastolic gallop). Gallop rhythms are usually most distinctly audible just medial from the apex of the heart, though the rhythm can usually be heard over the whole cardiac area.

The existence of gallop rhythm can be confirmed by palpation, inasmuch as the extra tone is accompanied by a *distinct shock palpable at the apex*. The tactile perception of the rhythm may be more definite than the acoustic perception

A gallop rhythm may be a normal phenomenon when third sound is audible.

It may be heard when a hypertrophied left ventricle is beginning to yield to the strain, and therefore its recognition may be more important for diagnosis and prognosis than that of a heart murmur.

HEART MURMURS. The heart sounds, normal or abnormal, and heart murmurs are noises, never pure tone.

The chief difference between the sounds in the normal and the abnormal heart and the heart murmurs lies in the duration, and in the termination, of the noises. The normal sounds are briefer, and they cease more quickly. Murmurs tend to be longer and to fade away gradually. These differences correspond to the origin of the sounds. The normal sounds arise from a single sudden disturbance of the equilibrium of the sound-producing body, whereas heart murmurs are due to a repeated disturbance.

In studying heart murmurs, attention is paid to (1) the time (or phase) in the cardiac revolution in which the murmur occurs, (2) the site at which the murmur is best heard and (3) the direction and propagation of the murmur. Less important features are (4) the intensity of the murmur, (5) its pitch and (6) its quality or timbre

Timing. The first determination to be made is the phase, or the phases, in the cardiac cycle in which the murmur is audible. All murmurs occurring between the beginning of the first sound of the heart and the end of the short pause marked by the beginning of the second sound are termed systolic murmurs All murmurs audible during the period extending from the moment at which the second sound begins to the end of the long pause marked by the beginning of the first sound are diastolic murmurs

The so-called presystolic murmur occurring just before the first sound of systole is in reality a diastolic murmur It is close to the normal systolic sound and far removed from the normal diastolic sound.

In fetal rhythms, when one of the heart sounds ceases to be audible, considerable difficulty may be experienced in timing a murmur. The best that can be done is to be guided by simultaneous auscultation and palpation of the apex beat or of the carotid pulse

In describing the position of a murmur, it is well to state where it is best heard and the direction of its conduction of propagation

Propagation As a rule, a murmur is best conducted in the direction of the flow of the current that produces it. It is desirable to ascertain not only the point at which a heart murmur is maximal but also the manner in which the murmur is propagated in one or more directions from this point. If, for example, a systolic murmur is produced by narrowing of the aortic valves (aortic stenosis), the murmur will be maximal at the auscultation site for that valve in the second intercostal space to the right of the sternum, and the murmur will be propagated upward toward the carotid and the subclavian arteries since this is the direction in which the blood flows from the narrowed spot at which the murmur arises.

If the aortic valves leak so that blood can pass back through them into the left ventricle during diastole (aortic regurgitation), the diastolic murmur will be propagated downward and to the left along the left margin of the sternum, corresponding to the direction of the regurgitant flow.

In narrowing of the mitral valve (mitral stenosis) the blood is forced through a narrow slit directly toward the apex of the heart, and during the period of the contraction of the atrium a systolic murmur in the region of the apex is heard. If the mitral valve leaks and blood regurgitates through it during contraction of the ventricles (mitral regurgitation), the murmur may be best propagated toward the apex of the heart, for instance in a direction opposite to the regurgitation. The murmur is sometimes best propagated toward the left atrium, and a systolic murmur may be audible either at the apex or in the pulmonary area.

When multiple heart murmurs coexist, a determination of the maximal and minimal points for each murmur and of the direction in which it is propagated is desirable.

If a murmur should be heard equally strongly in two areas, it is probable that an autochthonous murmur exists at each site, since a murmur propagated any distance is likely to be lessened in intensity.

In the presence of coexisting systolic and diastolic murmurs over the heart, the origin of the diastolic murmur is first located and analyzed, for diastolic murmurs are likely to be the most significant from the standpoint of diagnosis Subsequently the systolic murmurs may be analyzed for themselves

As a general rule, aortic murmurs are propagated toward the upper part of the body and mitral murmurs toward the lower.

Intensity Diastolic murmurs are usually less intense than systolic, though not always The two factors concerned in intensity are (1) the size of the opening and (2) the force, or velocity, of the flow. Care should be taken not to overestimate the importance of intensity for prognosis, for a very loud murmur may accompany a slight lesion, whereas a very soft murmur may coexist with a serious lesion of the heart With a given murmur, a patient's condition may be better when the murmur is intense than when it is feeble, since the intensity may vary with the force of the cardiac contraction

The intensity of a murmur increases and diminishes with the changes in blood pressure When a heart hypertrophies, the murmurs in it may become intensified, and when a heart weakens, the murmurs may grow feebler

The intensity of heart murmurs may also be influenced by posture. Most murmurs are more intense when the patient is in the recumbent position than when standing, the heart rate is less, and the ventricles contract more energetically.

The condition of the walls of a diseased orifice may affect the intensity of the murmur produced there Rigid, or calcified, valves may emit loud sounds, whereas soft, fresh thickenings of the valves may give rise to feeble murmurs

Quality According to the peculiar quality that heart murmurs manifest, they are designated as blowing, rasping, scratching, filing and musical, along with any other descriptive adjective the observer may desire to employ

Origin Under normal conditions the relations that exist among the cavities of the heart, the valvular orifices, the velocity of flow and the composition of the blood are such that no murmurs arise, but an abnormal condition of the orifices or a change in the velocity of flow or in the composition of the blood gives rise to murmurs

Significance A murmur audible over the heart may arise inside the heart (intracardiac murmur) or outside the heart (extracardiac or exocardial murmur). A murmur may be produced by organic disease of the heart valves (organic murmur), or it may be independent of such disease (functional heart murmur), or it may have its origin in conditions not due to disease of the heart muscle or its valves (accidental murmur), in which it may depend on changes in the physical state of the blood (anemic murmur) or on increased rapidity of flow (velocity murmurs in fevers) or on causes unknown

Organic Intracardiac Murmurs. Pathologic changes in the cardiac valves may lead to imperfect closure of the orifice, and this is designated valvular insufficiency A permanent narrowing of the orifice is known as valvular stenosis Murmurs due to insufficiency of a valve will be produced in those phases of the heart action during which the orifice is normally closed, whereas murmurs due to stenosis will arise when the orifice is open and the blood current is passing through it in the normal direction.

Functional Heart Murmurs Murmurs are frequently audible over the heart during life, though at necropsy no changes in the valves of the heart are demonstrable

Such murmurs, independent of anatomic lesions of the valves, are called functional murmurs. That a certain number of these are due to imperfect contraction of the muscle ring around the valve, leading to a relative insufficiency of the valvular closure, has been postulated Relative insufficiencies, if such exist, are common at the mitral and tricuspid orifices. They occur occasionally, but rarely, at the aortic orifice and perhaps also, though still more rarely, at the pulmonic orifice (Graham Steell murmur).

In all forms of anemia, especially in uncontrolled pernicious anemia, systolic murmurs may be heard over the whole heart; occasionally an anemic diastolic murmur is audible Perhaps some of the so-called accidental murmurs audible in cachexias may depend on the accompanying anemia.

In conditions in which the action of the heart is excited (fevers, neurasthenia, hyperthyroidism) systolic murmurs are often audible in the pulmonary region and over the left ventricle

A certain number of murmurs have their origin in the lungs during movements of the heart (cardiorespiratory murmurs)

The criterion for differential diagnosis between these less important murmurs and the more important murmurs due to organic disease of the valves or to relative insufficiency is not definite In general, the less important murmurs are systolic rather than diastolic. They are less precisely localizable than the organic murmurs. Many of them are heard in regions in which organic murmurs are rarely present

The less important murmurs are more variable in intensity than organic murmurs, especially under the influence of the respiratory movements and of change in posture Most important of all, they are not accompanied by those other changes in the heart and circulation that follow an organic disease of the valves.

Dorsal Auscultation According to Lian and Dang-van-Chung, diagnosis of certain cardiovascular disturbances cannot be established by auscultation of the anterior aspect of the thorax but may be elicited by auscultation of the back of the thorax This applies particularly to congenital stenosis of the aortic isthmus, in which a loud systolic murmur may be heard at the left omovertebral space. A systolic murmur can be heard along the left border of the vertebral column in the two inferior thirds of the left side of the thorax in cases of aneurysm of the descending aorta Dorsal auscultation may be an aid in the detection of continuous murmurs due to the compression of a branch of the pulmonary vein or to the presence of an intrapulmonary arteriovenous aneurysm An anterior mitral systolic murmur which is propagated to the back and is heard on dorsal auscultation is highly indicative of mitral insufficiency According to the site of its greatest intensity a systolic murmur at the base of the heart when propagated to the back and detected on dorsal auscultation may be of aid in the diagnosis and the localization of the causative lesion in the aorta (right supraspinous fossa) or in the pulmonary artery (left supraspinous fossa) The continuous murmur caused by the compression of the superior vena cava and that due to patent ductus arteriosus are propagated to the back only during systole Pericardiac friction sounds may be heard on dorsal auscultation in exceptional cases.

THE IMPORTANCE OF CARDIAC AUSCULTATION The importance of cardiac auscultation has been recently emphasized by Samuel A. Levine, who observes that if the competent examiner fails to hear any murmurs whatever, even with the patient turned to the left lateral and dorsal position or sitting upright, it can be safely assumed that subacute bacterial endocarditis or chronic rheumatic valvular heart disease is not present If a patient who has had rheumatic fever is examined one or more years afterward, and fever and murmurs are not observed, the heart sustained no important permanent damage. However, if in a patient who has had rheumatic fever, there is any kind of murmur, heart disease should be suspected If a diastolic murmur is present in any patient, the presence of organic valvular

disease must be suspected or at least cannot be dismissed, for auscultation is th only method of detecting early valvular heart disease. Likewise the detection c pericardial friction almost invariably means acute pericarditis and this may be firs demonstrated by auscultation.

In regard to particular valvular heart lesions, Levine calls attention to the fac that the presence of an *apical rumbling murmur*, diastolic or presystolic in time is diagnostic of mitral stenosis This murmur establishes the correct diagnosi even if it is faint or present only after effort or when the patient is lying on th left side A faint early diastolic murmur at the base of the heart is most significan in the diagnosis of early aortic insufficiency. In some instances auscultation is th only method which will aid in the diagnosis of either slight mitral stenosis o aortic insufficiency, for the roentgenograms and electrocardiograms may revea essentially normal conditions, and even symptoms of heart disease may be absen or equivocal

Emphasis in this discussion by Levine is in accord with that of other cardiologists that there *are many systolic murmurs, of which proper evaluation may be extremely difficult. It is well known that systolic murmurs may be heard in both valvular anc* nonvalvular disease of the heart and may be present in patients who are suffering from noncardiac disease or no disease at all. This does not detract from the value of auscultation In general a faint systolic murmur may be heard with or without heart disease but louder ones will seldom be present in normal persons and usually will indicate some form of heart disease

In a patient who has a severe epigastric pain of sudden onset in whom auscultation of the heart reveals a diastolic gallop, electrocardiographic studies usually will confirm the suspicion that the heart is the origin of the illness The detection of a snapping first sound while the heart rate is very rapid and grossly irregular in the absence of any murmurs is enough to arouse suspicion of the presence of mitral stenosis. Later, when the rate slows after digitalis therapy, the characteristic diastolic murmur may become audible A hyperactive first sound is present in thyrotoxicosis An exact doubling of the heart rate from 70 to 140 after brief effort arouses the suspicion of the presence of auricular flutter.

Many patients who display perfectly good or even loud first heart sounds are observed to have various forms of advanced cardiac disease, even with gross congestive failure. Others, on the contrary, who have faint and occasionally inaudible first sounds, are healthy

Levine has expressed the belief that in complete heart block, when the ventricles are beating very slowly and regularly and the auricles more rapidly, regularly and independently, the first sound varies greatly in intensity It is found to be loudest when P-R interval is exceedingly short and often the observer may be able to estimate the length of the P-R interval and to recognize conditions in which there is a short P-R interval, others with a prolonged P-R interval (first degree heart block) and those in which this interval is varying, such as second and third degree heart block In Levine's opinion, the detection of these changes in the intensity of the first sound is the only reliable bedside method of making these diagnoses If the heart rate is regular and the first sound decidedly decreased while the second sound is normal, the P-R interval will be at least at the upper limit of normal or delayed systole. Similarly, if the rate is regular and slow and the first sound changes in intensity with sudden loud explosive sounds, there is complete heart block with dissociation of the auricles and ventricles

Exocardial Murmurs. Abnormal sounds audible over the heart, synchronous with its action but arising *outside its cavities*, are (1) *pericardial friction* (see Pericarditis), (2) pleuropericardial friction, (3) cardiorespiratory murmurs, (4) precordial crackling characteristic of mediastinal emphysema (see Diseases of Mediastinum, Chapter 9) and (5) splashing sounds.

Pleuropericardial Friction Sounds A pulsatile friction sound, produced by rubbing of the outer surface of the pericardium against the pleura, may be synchronous not only with the heart's action but also with the respiratory movements. The portion of the sound due to the latter will cease when the breath is held.

Cardiorespiratory Murmurs These sounds arise in the lungs chiefly during the systoles accompanying inspiration. Occasionally diastolic sounds are produced and, sometimes, the sounds are audible during expiration also. The heart becomes smaller during systole and the ingress of air in the adjacent lung is increased, owing to greater negative pressure in the lung. The sounds may be blowing, like those of vesicular breathing, or crackles and rales may be produced. The systolic vesicular breathing may closely resemble a heart murmur These pulsatile pulmonary sounds usually cease, or are markedly modified, when the breath is held They are also much influenced by changes in posture.

When the lung is adherent in front of the vessels at the base of the heart, a diastolic murmur sometimes becomes audible, the diastolic retraction of the aorta causing a localized aspiration into the adjacent pulmonary alveoli.

Splashing Sounds. If the air and fluid occur together in the pericardial cavity, each beat of the heart may give rise to a metallic, ringing splash Similar sounds are sometimes heard when there is a pulmonary cavity near the heart, when a hydropneumothorax exists, or even when the stomach is much distended with fluid and gas

If sounds have an extrapericardial origin, they will disappear when the patient is sitting, to reappear when he lies down, but if they have an intrapericardial origin, the sound is heard in both positions

AUSCULTATION OF THE BLOOD VESSELS When one is listening over the blood vessels, care must be exercised not to exert pressure with the stethoscope, otherwise a narrowing of the vessel will be produced which will give rise to a murmur.

Auscultation of the Arteries The observer locates the vessel by palpation and sets the bell of the stethoscope lightly upon it. Normally two sounds are audible in the subclavian and the carotid arteries, the first just after the beginning of ventricular systole, the second just after the beginning of ventricular diastole. If the artery is pressed on now with the stethoscope, a ventriculosystolic stenosal murmur will become audible. No sounds are audible, normally, over the other arteries of the body

Systolic murmurs due to narrowing at the aortic orifice are often propagated into the carotid and the subclavian arteries When the aortic second sound is absent, as in some cases of aortic insufficiency, no arteriosystolic tones are heard in the great vessels.

When a Corrigan pulse exists, the pulse wave rising quickly and sinking again very rapidly, murmurs are often audible in the arteries of the neck and in the femoral and the brachial arteries The phenomenon is most often met with in aortic insufficiency but it may also be encountered in hyperthyroidism, in fever, and in nervous palpitation When a very loud sound is audible, it is spoken of as a pistol-shot sound

In aortic insufficiency, on listening over the femoral artery, two tones, quickly following one another, are sometimes to be heard (Traube's double tone) On slight pressure with the stethoscope these tones disappear, and first is heard a normal pressure murmur and, later, on stronger pressure, a second murmur (Duroziez's double murmur) Duroziez's double murmur is hard to differentiate from the normal pressure tone

Any compression of an artery may give rise to a stenosal murmur, for example, this fact is utilized in the auscultatory method of determining maximal and minimal blood pressure.

Auscultation of the Right Jugular Vein. The stethoscope is placed over the sternal attachment of the right sternocleidomastoid muscle, the patient sitting or standing with the head turned toward the left.

In the jugular vein certain sounds become audible under abnormal conditions, they include (1) the venous hum and (2) the venous tone.

In anemic patients, and occasionally in healthy persons, a continuous blowing, singing or humming murmur, with systolic accentuation heard over the jugular vein, is a venous hum Less continuous, more intermittent, venous murmurs are unimportant

Venous tone is occasionally audible, in the same situation, in tricuspid insufficiency; it is due to sudden tension of the dilated vein when the blood propelled by the contracting right ventricle rushes into it.

Movements of the Heart and Blood Vessels. The signs of the activity of the heart include the heart sounds (page 644), and certain movements of the heart and blood vessels that are accessible to clinical examination. These movements are visible and palpable as pulsations in the heart and its neighborhood and in the arteries and veins of the body. The movements can be most accurately analyzed by means of instruments of precision yielding graphic records.

With the hand most of the movements which can be seen can be felt, and a number of movements that cannot be seen are recognizable by *palpation*. Thus, for example, an apex beat that is invisible may sometimes be felt; various invisible shocks and thrills are palpable; and, in addition, details of the movements of the blood vessels that are not accessible to inspection can be made out on palpation

In practicing palpation, the palm of the hand (the tips of fingers for the pulse) is applied lightly and with varying degrees of pressure on the area to be examined. The region of the apex of the heart first, and successively the whole precordial area, the axillae, the vessels in the neck, the epigastric and hepatic regions and the more superficial vessels in various parts of the body, including, of course, the vessels of the feet, are palpated

Low-pitched murmurs are the ones that favor the formation of thrills, whereas those that yield rapid vibrations producing high-pitched murmurs may not give rise to palpable thrills This explains why a thrill may sometimes be felt when a murmur is not audible or is a very indistinct rumble and why the loudest and most distinct blowing murmurs may be unaccompanied by thrills. Palpation and auscultation here supplement one another advantageously in diagnosis

Abdominal Pulsations. Pulsation, due directly or indirectly to the heart, is present in the epigastric fossa, in the neighborhood of the xiphoid process between the two costal margins It may depend on (1) the abdominal aorta or (2) the right ventricle

The commonest aortic form is that met with in neurasthenics and emaciated dyspeptics with thin, loose abdominal walls, the so-called dynamic aorta This pulsation is slightly to the left of the middle line and extends for a variable distance downward, below the xiphoid process The pulsation is perpendicular from behind forward, has only a slight breath and is somewhat later than the apex beat. One tone, or a systolic murmur, may be audible on auscultation The pulsation is increased by anything that excites the heart's activity. In many cases in which this form of aortic pulsation is present, the aorta can be grasped in the palpating hand, which then becomes aware of marked lateral expansion with each pulsation In such cases, however, the aorta can be palpated lower down and the same condition found; there is never a localized expansile tumor such as is present in aneurysm of the abdominal aorta

Epigastric pulsations due to the right ventricle itself may be either systolic elevations or systolic retractions Systolic elevations are usually due to a lowered

and enlarged right ventricle (pulmonary emphysema, dilated right heart, right heart failure, cardioptosis).

Systolic retractions in the epigastrium, due to the right ventricle, are rather diffuse, wavelike movements depending on elevation of the diaphragm by the contracting right ventricle; they are of no clinical significance except when there is failure of the right side of the heart.

VISIBLE PULSATIONS Visible pulsation of the peripheral arteries occurs in aortic insufficiency For the characters of the arterial pulse, however, reliance is made on palpation.

Pulsations in the veins of the neck may be visible in health, though they are much more often seen in disease. A normal venous pulse when visible presents two waves recognizable by the eye, both diastolic. Palpation is of little value in the study of the venous pulse.

A visible capillary pulse is met with in conditions associated with hypertrophy of the left ventricle, especially in aortic insufficiency If a line is scratched with the fingernail on the forehead or on the skin of the trunk, or if light pressure is made on the end of the patient's fingernail in order to make a pale spot in the nail bed, the borders of which may be closely watched, alternately blush and pallor synchronous with the pulse are revealed if a capillary pulse exists A very good way to look for a capillary pulse is to press gently with a glass slide on the lips Sometimes, a blush of the cheek can be seen with each systole of the heart.

THE PULSE By pulse is meant the pressure wave of enlargement of the artery which occurs at each systole of the heart and which takes a perceptible time to travel from the heart to the periphery. Attention is paid to the following qualities: (1) the frequency, (2) the rhythm, (3) the volume, (4) the quickness or celerity, (5) the tension and (6) the equality on the two sides of the body

The thickness of the vessel, which is usually attended to at the same time, is not a pulse phenomenon, but has to do with the condition of the arterial wall itself.

Rate. This varies in healthy adults between 60 and 90 beats per minute; in children, 90 to 140, in old age, 70 to 90. The pulse is faster in women than in men On sitting or on lying, the pulse is slower than on standing or on exercising

Acceleration of the pulse rate is due to cardiac hurry or tachycardia It is met with normally on exertion, during emotion, pain, fever, and after taking food

In hyperthyroidism, and in some neurasthenic states, tachycardia is common A frequent pulse is often an important sign of cardiac weakness or collapse. In paroxysmal tachycardia, attacks of great frequency of rate having a sudden onset, and ceasing suddenly, are met with, alternating with periods of normal frequency. The attacks may last from a few minutes to several days, the pulse beats often numbering between 140 and 280 per minute

Slowing of the pulse rate is known as bradycardia It is met with in convalescence from many infectious diseases, especially typhoid fever, influenza and pneumonia, in disturbances of digestion, in conditions in which the vagus centers are stimulated (brain tumors, hydrocephalus, beginning meningitis), in icterus and in various diseases that affect the heart itself (aortic stenosis, coronary sclerosis, myocarditis). In Adams-Stokes syndrome, in which the stimulus from the sinus and auricles is prevented from reaching the ventricles, the latter contract in their own independent rhythm, in these cases the arterial pulse rate may fall below 30

Rhythm Normally the single pulse waves follow one another regularly, but in pathologic conditions the rhythm may become irregular The irregular pulse is due to cardiac arrhythmia Under this heading there are included (1) respiratory irregularities, (2) extrasystolic irregularities, (3) heart block, (4) perpetual arrhythmia and (5) the alternating pulse

Volume. What clinicians speak of as the volume of the pulse is dependent chiefly on the difference between the increase in pressure during ventricular systole and

the decrease in pressure during ventricular diastole. The size of the pulse waves depends chiefly on (1) the volume of the systolic output of the left ventricle and (2) the ease with which blood flows out of the arteries through the capillaries. The volume of the pulse is, therefore, the palpatory equivalent in the radial artery of what is known as the pulse pressure (difference between maximal systolic and minimal diastolic pressure).

If the pulse wave rises very quickly and falls rapidly, it is spoken of as a water-hammer pulse (Corrigan pulse).

Tension This is judged by the force required to obliterate the pulse when the fingers press on it Three fingers are placed on the radial artery, the most pressure is applied with the distal finger hard enough to prevent a recurrent pulse wave through the palmar arch, pressure is then made with the most proximal finger until the pulse ceases to be perceptible to the finger in the middle. If difficult to compress, the pulse is said to be of high tension, when easily compressible, it is of low tension

Equality. The commonest cause of differences in the pulse in the two radial arteries is the presence of an abnormally small radial artery on one side. This is a common anomaly in the arterial system of the forearm. As a result the pulses vary chiefly in absolute volume, they are equal in time. In aneurysm of the arch of the aorta, or of one of the arterial trunks supplying the arms, differences in the time as well as in the volume and tension of the two pulses are prominent

Changes in the Cardiac Rhythm. The clinical significance of changes in the cardiac rhythm, especially the cardiac arrhythmia, has been greatly clarified by the studies of Thomas Lewis and by the use of electrocardiograph Increase in the cardiac rhythm beyond the limits of the normal number of heart beats per minute is tachycardia Decrease in the cardiac rhythm below the limits of the normal number of heart beats per minute is bradycardia

The *tachycardias* with a *regular pulse* rhythm, as proved by the electrocardiogram, include sino-auricular tachycardia, paroxysmal auricular tachycardia, ventricular tachycardia and most instances of auricular flutter. Tachycardias with an *irregular pulse* rhythm include auricular fibrillation and sinus tachycardia with premature beats.

Bradycardias with *regular pulse* rhythm include sinus bradycardia, nodal rhythm, constant partial heart block and complete heart block. *Irregular bradycardias* include sino-auricular bradycardia with frequent premature beats and partial heart block with frequent dropped beats

Irregular rhythms with normal heart rate are found to include premature beats, auricular fibrillation with ventricular rate slowed by digitalis, sinus arrhythmia and partial heart block with dropped beats

In *sinus tachycardia* the cardiac impulse as recorded on the electrocardiograph arises normally in the sino-auricular node The heart rate is increased Since the heart rate of normal individuals varies greatly, it is well not to interpret an increased pulse rate as being abnormal until it is known whether the particular rate is abnormal for the patient in question. The origin of the activating impulse is revealed by the electrocardiograph. If the impulse arises in a ventricular focus, it causes ventricular premature beats. If the impulse arises above the bifurcation of the bundle of His, it causes supraventricular premature beats. In supraventricular premature beats the impulse arises in the auriculoventricular node and thus the beats are termed nodal premature beats. If the impulse arises elsewhere in the atria, there are auricular premature beats.

In tachycardias there may be no subjective symptoms, or there may be disagreeable palpitation, fatigue and breathlessness

Examination of the heart and pulse discloses a regular rhythm with a rate exceeding 90 to 100, but less than 160, per minute Differentiation from other tachycardias with regular rhythm may be surmised or made from the electrocardiogram.

In *sinus bradycardia* the cardiac impulse arises normally in the sino-auricular node as revealed by the electrocardiograph. Symptoms of sinus bradycardia are absent except in the extremes, when there is dizziness, faintness or syncope. Syncopal attacks if they occur may be due to cardiac asystole. Examination of the heart and pulse discloses a regular rhythm with slowing of the heart rate below 60 per minute.

In *sinus respiratory* or *juvenile arrhythmia* the cardiac impulse arises normally in the sino-auricular node as revealed by the electrocardiograph and the arrhythmia is characterized by alternating periods of slower and more rapid cardiac rates which are usually related to respiration. The heart rate increases with inspiration and diminishes with expiration

Sinus arrhythmia is recognized clinically by regular but more rapid heart beats during inspiration and slower beats during expiration The periodic variation in the rate is intensified by deep breathing and stopped by breath-holding or by exercise. A sinus arrhythmia is of no clinical importance

In *sinus arrest* (sino-auricular standstill or sinus pause) there is momentary failure of the sinus node to initiate an impulse. The failure is caused usually by digitalis or quinidine intoxication Clinically the rhythm is regular, but there is slowing of the pulse. An electrocardiogram is essential for diagnosis.

When heart beats are controlled by the *auriculoventricular node*, there is a shifting pacemaker Auriculoventricular rhythm occurs relatively infrequently. It is almost always a transient phenomenon alternating with sinus rhythm Clinical symptoms are uncommon and rarely distressing. Diagnosis requires electrocardiographic study

When there is shifting of the pacemaker, there may be *reciprocal beats,* that is, there is an auriculoventricular rhythm in which the ventricles contract before the atria The atrial activation is delayed long enough so that the ventricles can respond to the returning auricular (nodal) impulse This phenomenon is often induced by pressure on the carotid sinus or digitalis therapy Diagnosis is by electrocardiogram

In other instances of a shifting of the pacemaker there may be *auriculoventricular rhythm* and *auriculoventricular dissociation*. In auriculoventricular dissociation there are responses to different pacemakers The ventricular rate, controlled by the auriculoventricular node, may exceed that of the atria which are responding to a depressed sino-auricular node This type of auriculoventricular dissociation is usually the result of digitalis, or of infections such as rheumatic fever In this condition the dissociation results from complete auriculoventricular block The electrocardiogram is necessary for diagnosis

Premature beats or extrasystoles are cardiac contractions of ectopic origin which occur earlier than expected in the dominant or usual rhythm They are distinguished electrocardiographically by their point of origin, for instance auricular, auriculoventricular or nodal, and ventricular premature beats

When there is recurrently a normal beat followed by an extrasystole, the rhythm is coupling of beats (bigeminal pulse) Bigeminal pulse is induced by two beats in close proximity followed by a long compensatory pause. The commonest type of coupling is due to alternate extrasystoles and is caused by digitalis Coupling of beats may also result from partial auriculoventricular block, not the result of digitalis, in which every third beat (trigeminal pulse) is dropped and thus a 3 2 sino-auricular block exists If every fourth beat is blocked, there is a 4 3 sino-auricular block

The majority of patients who have premature beats do not have organic heart disease The presence of heart disease may increase the occurrence and frequency of premature beats. In those who have premature beats and do not have heart disease, emotional stress and conflict, mental or physical fatigue, irregular sleep and digestive disturbances, especially when these are combined with excessive smoking of tobacco or drinking of alcohol or coffee, increase the beats.

Premature beats occur at all ages. After the age of 50 years, the freque creases, and after 70 years, premature beats are very commonly present Al patient is aware of premature heart beats, there may be a sensation of stopj the heart, momentary faintness, or dizziness, and anxiety. The patient may d palpitation as an oppression, fluttering, thumping, skipped beats, or a sinkir ing Occasionally the discomfort is localized in or extends to the neck, wh patient experiences a sensation of fullness, tightness, pulsation or wave reacl the top of the head. This may be caused by the regurgitant stream from th atrium to the veins of the neck when the atrium contracts simultaneously w ventricle and the tricuspid valve is closed

During the occurrence of a series of extrasystoles there may be anxiety, sweating, nausea, weakness, dizziness, faintness and breathlessness

Premature beats often become annoying when the patient retires for the Conversely, exercise or anything which increases the heart rate eliminates tl mature beats

Premature beats are recognized by auscultation, occasionally by palpat the radial pulse. They may be absent at the time of physical or electrocardiog examination The electrocardiogram is essential for definite diagnosis and lo tion of premature beats.

A ... *cardia is manifested by a rapid but regular* rate ... rhyth ... node in its pathway.

The etiology of auricular paroxysmal tachycardia is obscure, but it seem organic heart disease is usually absent Auricular paroxysmal tachycardia occ any age, including infancy It is commonest between 20 and 40 years of age

Paroxysms of brief duration may be accompanied by mild palpitation symptoms at all. In the severer attack there is sudden onset with a thump c against the thoracic wall, followed by cutaneous palpitation, fluttering, raci pumping of the heart beat Often there are stenocardia and smothering sens: or epigastric distress

The psychic and reflex nervous manifestations may be profoundly express angor animi, syncope, anxiety, weakness, exhaustion, coldness, sweating, dizz and faintness Abdominal distention, gaseous eructations, salivation, naus vomiting, or polyuria may terminate the attack

It is remarkable how often heart rates of more than 200 per minute in p ... for hours or days without evidence of circu ... restored ... in ... there is organic disease it is ... 's fa

In the extreme and very exceptional instance the attack is prolong . In case there may be peripheral slowing of the circulation to the extent that throm and gangrene of an extremity occur. The attacks can terminate fatally, either signs of progressive failure or suddenly

On physical examination the only abnormality is a regular and constantly heart rate. In those who have organic disease there may be cardiac enlargemen murmurs.

In most cases auricular paroxysmal tachycardia is of no clinical import either from the viewpoint of producing disturbing symptoms or from that o noting the presence of organic heart disease, except in very rare instances in v the paroxysms recur frequently or are very prolonged.

The most useful therapeutic and often diagnostic procedure is to make pre over the right carotid sinus and, if this is ineffective, over the left carotid sinu

10 to 30 seconds. The carotid sinus may be located by feeling the strong carotid arterial pulsations at the bifurcation of the common carotid artery at the level of the upper border of the thyroid cartilage. The patient may be reclining or sitting with his head slightly forward and his neck relaxed. Pressure is best made with two or three fingers, compressing the artery and sinus posteriorly and medially against the vertebral spine. Occasionally a massaging motion is effective. Prolongation of the procedure is avoided because of the possible risk of syncope or cardiac standstill.

Auricular flutter is due to a mechanism related to auricular fibrillation or auricular tachycardia—a circus rhythm.

In auricular flutter the atria beat regularly at a rate of 250 to 350 per minute. As a rule, however, there are varying degrees of partial heart block (2:1, 3:2, 3:1, and others) Most commonly the ventricular rates vary between 100 and 150 per minute and there is a 2:1 block. With higher degrees of block, for example, 4:1, the ventricles may beat not only regularly but at normal rates, 70 to 80. In infants and rarely in adults there is a 1:1 ventricular auricular rate.

Auricular flutter does not necessarily indicate heart disease. However, it is often associated with mitral stenosis, and it may be present with hyperthyroidism, coronary arteriosclerotic disease and hypertensive heart disease. Auricular flutter may be associated with mediastinal disease, and may occur during surgical procedures in the thoracic cavity.

The symptoms of auricular flutter are sudden tachycardia, palpitation, fear of impending death, weakness, dizziness and syncope, and in some cases there are the symptoms and signs of congestive heart failure or shock

Auricular flutter is often more disturbing to the patient than auricular tachycardia because of its greater tendency to persist (days, weeks, months or years). Auricular flutter is likely to be followed by auricular fibrillation. In auricular flutter the pulse is regular.

Auscultation of the heart discloses apical rates which depend on the degree of heart block (2:1, 3:1 or 4:1). Sudden changes in rates indicate changes in the degree of the block Exercise may raise the ventricular rate and induce a constant degree of block and a regular heart beat.

The diagnosis is established by means of electrocardiographic studies

Auricular fibrillation is an irregular irregularity of the heart beat Like auricular flutter, it is regarded as a circus rhythm of an ectopic stimulus. In auricular fibrillation, however, the basic circuit is shorter and the frequency of circulation of the excitation wave is greater than in flutter.

Auricular fibrillation is associated with various degrees of auriculoventricular block. The auricular rhythm is irregular, the ventricular rhythm also in auricular fibrillation is irregular

Auricular fibrillation is commonly associated with severe organic heart disease. It may be present, however, in patients who have apparently otherwise normal hearts Auricular fibrillation occurs most commonly in rheumatic heart disease, coronary arteriosclerotic heart disease with heart failure, and hyperthyroidism Paroxysmal auricular fibrillation is particularly identified with hyperthyroidism, although it may occur in any type of heart disease, including congestive heart failure as well as subacute bacterial endocarditis It may occur in paroxysms in the first two weeks after an acute myocardial infarction, but in the latter condition it usually subsides spontaneously after several hours Most frequently auricular fibrillation is observed in patients more than 40 years old Women are more commonly affected in the younger age period, that is, in hyperthyroidism and mitral stenosis, men, in coronary artery disease and hence in the older age periods

Often the onset of permanent auricular fibrillation impairs the cardiac sufficiency to a degree that heart failure is chronic thereafter In any patient who has auricular

fibrillation, auricular thrombosis may occur. However, thrombus formation and subsequent infarctions are common in mitral stenosis, with or without auricular fibrillation

The heart rate and the pulse rate possess the quality of irregular irregularity In rapid ventricular rates the pulse rate is considerably less than the apical rate; this difference is termed a pulse deficit The pulse deficit results from failure of many of the weak ventricular beats to expel a sufficiently large column of blood to reach the radial artery The pulse deficit is increased by the inability of the counter to count weak pulse beats which are closely spaced.

In those individuals who have pulse deficits the diagnosis is made by this finding In all cases electrocardiographic studies are necessary for a diagnosis.

In an otherwise normal heart paroxysmal auricular fibrillation may be disturbing, but it is usually of no importance as regards the outlook for life or the development of heart disease

In the presence of organic heart disease a persistent auricular fibrillation is an unfavorable occurrence

Treatment for a *paroxysm* of auricular fibrillation is indicated only if the paroxysm is associated with distressing and prolonged palpitation, evidences of heart failure or of cerebral or peripheral ischemia.

In all other instances, if treatment for auricular fibrillation is necessary, it consists essentially of the use of digitalis or quinidine

Ventricular tachycardia is a rapid, regular rhythm initiated by stimuli arising in an ectopic focus in the ventricular conduction system The ventricular rate varies usually between 150 and 300 per minute. The atria may contract regularly and normally or may respond to retrograde conduction along the auriculoventricular bundle and node, while the ventricles respond to the ectopic ventricular stimulus.

Paroxysmal ventricular tachycardia is most often associated with recent myocardial infarction It may occur without myocardial infarction in association with hypertensive and arteriosclerotic heart disease after excessive exertion and after excessive administration of digitalis Occasionally, however, ventricular tachycardia is observed without evidence of organic heart disease.

The symptoms of ventricular tachycardia are identical with those of auricular paroxysmal tachycardia The diagnosis depends on the electrocardiographic studies

Ventricular tachycardia is a serious condition. Ventricular tachycardia with alternating direction of the ventricular complexes has been considered especially ominous and almost invariably fatal In some patients who do not have organic heart disease other than the arrhythmia, the prognosis is good. Administration of quinidine constitutes the treatment.

Ventricular fibrillation is observed as the result of myocardial infarction, general anesthesia, lightning shock, digitalis or quinidine, and as a terminal event in a variety of diseases. It is likely due to an inconstant circus rhythm

Ventricular fibrillation probably occurs more frequently in those who have not had heart disease than in those who have had it, for it is the terminating event in the lives of many individuals In heart disease it is the terminating event in angina pectoris, and in acute coronary occlusion and syphilitic aortitis The intravenous injection of drugs is often responsible for this serious cardiac arrhythmia. Faintness occurs when ventricular fibrillation lasts 3 seconds, syncope after 10 to 20 seconds, and convulsions, apnea and incontinence after 40 seconds.

Electrocardiographic studies are diagnostic if life is sufficiently prolonged to make the diagnosis If ventricular fibrillation is not immediately fatal, the patient may recover.

Heart block results from aberrations in the sino-auricular node, auriculoventricular node, bundle branch and short P-R interval with prolonged QRS complex.

Sino-auricular block may result from vagal stimulation, for instance a sensitive carotid sinus, tumors compressing the carotid sinus, vagal reflexes during anesthesia and surgical procedures, and cerebral lesions The usual cause, however, of sino-auricular block is poisoning by digitalis and occasionally quinidine

There are usually no clinical symptoms unless there are frequent and prolonged pauses However, in prolonged pauses there may be dizziness or faintness, and even attacks of the Adams-Stokes syndrome may occur Death resulting from cardiac standstill is not expected.

Sino-auricular block is distinguished by the electrocardiogram It is treated by stopping the administration of the heart medicine.

In *auriculoventricular block* there is a delay in transmission of the impulse through the auriculoventricular node and bundle, or an interruption of an occasional impulse or of all impulses in either the node or the bundle. Thus there are variations in degree of heart block from none at all to complete block.

Complete heart block is a common disorder of the heart beat, appearing in recurrent attacks, often leaving normal conduction between attacks The frequency of heart block is exceeded only by that of premature beats, auricular fibrillation and auricular paroxysmal tachycardia.

Complete heart block may be transient or permanent and it may represent a functional or an organic disturbance.

Coronary arteriosclerosis, rheumatic heart disease, syphilitic heart disease, neoplasms and congenital heart disease, and effects of the common drugs (digitalis, quinidine) used in therapy are the usual causes of heart block. Occasionally heart block is caused by acute infectious diseases, notably rheumatic fever and diphtheria, but at times by almost every other infection

In most instances of heart block associated with acute infections there is only a prolongation of the P-R interval In such cases the P-R interval may often be shortened to normal by the administration of atropine.

In the normal electrocardiogram the P-R interval varies between 0.12 and 0 2 second At slow cardiac rates (60 per minute or less) a P-R interval up to 0 21 or 0 22 may be normal In prolonged auriculoventricular conduction time the P-R interval exceeds 0 2 second In partial heart block there periodically is a dropped beat The P-R interval may increase progressively until a QRS is omitted, until the ventricles respond only to every second, third, or fourth beat, resulting in 2:1, 3·1, or 4.1 block

There are no symptoms The heart rate increases with exercise or excitement

In complete heart block there is the virtual regularity of atrial and ventricular activity with continual variation in the P-R interval The auricular rate is increased over the ventricular rate and both rhythms are essentially regular

In complete heart block the *Adams-Stokes syndrome* may occur The Adams-Stokes syndrome results from a prolonged systole of 5 to 10 seconds or more As the result the patient becomes pale and pulseless, and loses consciousness When the asystole lasts for 15 seconds or more, there is cyanosis, and respirations are deep and labored, or of the Cheyne-Stokes type There is a generalized convulsive seizure which lasts for a minute or longer Then the convulsive movements cease, and the pulse and respirations return to normal The color is restored Paroxysms longer than a minute may be fatal. Recovery may follow longer periods of asystole.

In partial or complete heart block the cardiac rate is slow, 50 to 40 per minute or less The lower rates prevail in complete heart block that is congenital, rheumatic, or due to digitalis

In complete heart block variations in the intensity of the first heart sound may

be heard. The auricular sound sometimes may be heard faintly between the regular heart sounds, or there may be reduplication of the first or second sound which may be thought to be auricular sounds.

The clinical significance, treatment, and the prognosis of heart block depend on the causative factor

In *bundle-branch block* there is a delay in or an obstruction to the conduction of impulses through one of the branches of the bundle of His, or there are obstructions in the Purkinje fibers.

Left and right bundle-branch blocks are identified. Left bundle-branch block occurs more frequently than right bundle-branch block.

The great majority of instances of bundle-branch block (left bundle branch) are due to coronary arteriosclerosis and associated hypertension The bundle branches are often damaged or blocked by cardiac infarction and degenerative changes secondary to myocardial ischemia

There are no symptoms of bundle-branch block. The definite diagnosis depends on the revelations of the electrocardiogram.

Blood Pressure. MEASUREMENT OF BLOOD PRESSURE Clinically the arterial pressure in the brachial artery is measured routinely. The maximal arterial blood pressure or systolic pressure is recorded as the highest point reached by the blood pressure in the artery during the ventricular systole. The minimal arterial blood pressure or diastolic pressure is recorded as the lowest point reached by the blood pressure within the artery during ventricular diastole

If the minimal blood pressure is substracted from the maximal blood pressure, the remainder is known as the pulse pressure. The term mean pressure is used to designate the average pressure *during a certain period*.

The principles underlying all the instruments for determination of blood pressure are the same The arterial pulse is obliterated by compression from without by means of a cuff, and the pressure necessary for compression is measured by some form of manometer. These instruments include the mercury manometers and aneroid manometers. The mercury manometers are preferable for office use. The aneroid manometer is convenient for bedside use, being small and easily portable. It may require, however, to be adjusted, at intervals, on comparison with a mercury manometer

ARTERIAL BLOOD PRESSURE. A cuff is applied over the brachial artery, and the pressure in it is raised until the radial pulse disappears The bell of the stethoscope is then placed over the artery close to the cuff, the position of the bell is the antecubital space It is customary to speak of five distinct phases as the sound varies during the fall of the pressure in the cuff.

First Phase When the pressure falls to the level of the maximal systolic pressure, an arterial tone is heard, not unlike the first sound of the heart It is due to the return of the pulse wave in the artery, the vibrations being supplemented by the resonance of the air within the cuff This is the maximal (systolic) pressure.

Second Phase As the pressure in the cuff falls further, the sound of the first phase is accompanied by a hissing murmur as the blood flows through the constriction into the wider artery below

Third Phase. As the minimal diastolic pressure is approached, the murmur of the second phase disappears, and a tone, usually much louder than that of the first phase, becomes audible.

Fourth Phase. At the end of the third phase, if the examiner listens attentively, the sound will be observed to become diminished suddenly and markedly and to assume a muffled character. The onset of this fourth phase formerly was considered to indicate the exact moment at which the pressure within the cuff corresponds to the minimal (diastolic) pressure in the brachial artery. Recently, however, a committee chosen by the American Heart Association has decided that in clinical practice the recorded diastolic pressure shall be the reading of the manometer at the end of the fif[illegible] hase.

Fifth Phase This is very short, at the end of it the sound disappears entirely This is now considered to be the diastolic pressure However, this arbitrary standard for diastolic pressure remains with the one limitation of all auscultatory methods. It is somewhat unsatisfactory when tones are audible in the peripheral arteries before the cuff is applied (for example, in aortic insufficiency).

CLINICAL ESTIMATION OF BLOOD PRESSURE The recorded level of blood pressure, in addition to individual fluctuation, is affected by numerous technical circumstances, such as the nature of the apparatus and whether the measurement is made by auscultation or by palpation In a study of the accuracy of blood pressure recordings, Ragan and Bordley compared auscultatory pressure measurements with intra-arterial pressure measurements 138 times in 51 adult subjects They found that the agreement between the auscultatory and intra-arterial measurements of systolic pressure was affected both by the size of the subject's arm and by the contour of the pulse wave They concluded, therefore, that the commonly employed clinical method of measuring blood pressure should not be considered a truly accurate procedure and that misinformation is particularly likely to be obtained in subjects who have unusually large or unusually small arms If the arm is small, the clinical estimate of the systolic pressure is likely to be too low, if the arm is large, the clinical estimate of both systolic and diastolic pressures is likely to be too high. The error in either direction may exceed 30 mm. of mercury. The error can be reduced in large-armed or fat-armed individuals if the width of the cuff is increased as it is in the cuffs for leg pressures In small-armed adult persons and in children the error can be reduced by the use of successively narrower cuffs

THE RANGE OF NORMAL BLOOD PRESSURE Master and associates record that the normal range of systolic blood pressure in men starts at the age of 16 years with 105 to 135 mm of mercury, and at ages 60 to 64 years reaches 115 to 170. In women it starts at a slightly lower level, at 16 years of age the normal range is 100 to 130 mm of mercury At ages 60 to 64 years the range is 115 to 175 This is slightly higher than in men

In men at ages 16 to 18 years the lower limit of hypertension is 145 mm. of mercury systolic; at 19 years, 150 mm., and at 30 to 34 years, 155 mm It then increases about 5 mm every five years At ages 60 to 64 years, 190 mm is the lower limit In women the lower limit of hypertension is 140 mm. of mercury systolic up to age 30 years Thereafter it increases 5 or 10 mm for every five years, and by age 45 years it is actually higher than in men The hypertensive limit remains higher than among men up to ages 60 to 64 years, when it may be taken as the same in the two sexes

The range of normal diastolic pressure begins at 60 to 86 mm of mercury at age 16 years in men and at 65 to 85 mm in women The change with age is gradual. By ages 40 to 44 years the level is 70 to 94 mm for men, after age 40 years the lower limit of normal remains the same, but the upper limit of normal gradually increases to 100 mm at ages 60 to 64 years In women the normal range at 40 to 44 years is 65 to 92 mm. and at ages 50 to 54 years rises to 70 to 100 mm ; it remains at this level to 60 to 64 years of age

Mean blood pressure readings, both systolic and diastolic, increase with age in both sexes Average systolic readings for men show a fairly smooth progression up to the age of 50 years, after that age the increase accelerates For women the increase in the averages by age is somewhat less smooth or continuous than it is for men, but among them, too, it is accelerated after the age of 50 years. Beginning with age of 20 years the upward progression in diastolic pressure with age is fairly steady for both sexes, systematic acceleration of the average is not found over any broad age period

Among boys between the ages of 16 and 19 years, an upward trend is observed in the averages for both systolic and diastolic pressures. Among girls, on the other

hand, values for both systolic and diastolic pressure are practically identical between the ages of 16 and 18 years and remain unchanged through the age period 19 to 24 years Explanation of this difference may lie in the fact that boys mature between the ages of 16 and 19 years, they become heavier and are much more active than are girls at these ages. Girls mature earlier. It has been long recognized that a rapid rise in blood pressure occurs during puberty and adolescence.

No clear-cut relationship between height and blood pressure has been established

Weight is an important and consistent factor in blood pressure changes. With increase in weight there is progressive increase in the averages in systolic and diastolic blood pressure, regardless of age or sex.

The difference in the mean systolic blood pressure of underweight and overweight groups at each extreme exceeds 10 mm of mercury in some instances; the difference in diastolic pressure is almost as great. Among women, particularly after the age of 40 years, the differences between the weight groups at either extreme with respect to the mean pressures, both systolic and diastolic, are even greater than are those among men Absolute and relative variations in blood pressures, as measured by the standard deviation and the coefficient of variation, also tend to increase with weight, particularly after the age of 40 years. In general, the greatest contrast in the mean pressure is found at the older ages and among women.

Blood Pressure Variations in the Two Arms In 1,388 blood pressure readings Rueger found the blood pressure to be the highest in the right arm in 992 readings, as compared to 274 in the left arm, and to be equal in both arms in only 122 readings. The systolic variation in the two arms was 10 or more points in 694 readings, and zero to 10 points also in 694 readings, out of the total of 1,388 tabulations The diastolic variation in the two arms was much less marked, with 920 readings showing less than 10 points difference, as compared to 468 readings showing a difference of 10 or more points

Casual and Basal Blood Pressures. Smirk defines casual blood pressure as the sum of the basal blood pressure and the supplemental pressure; this last represents the degree of blood pressure elevation above the basal level due to whatever degree of physical, emotional and suprabasal metabolic activity is present at the time of blood pressure measurement The basal pressure is the pressure measured at a time when physical, emotional and metabolic activity are reduced to a physiologic minimum Failure to obtain the true basal reading will not always be apparent to the observer, especially when the failure is due to emotional reasons Both normal and hypertensive subjects with a high basal pressure have a greater statistical expectation of having a high casual pressure than do those whose basal pressure is low. Likewise those with high supplemental pressures have a greater statistical expectation of a high casual pressure than do those whose supplemental pressure is low. In comparing one individual with another, the basal and supplemental pressures [illegible] are independent variables in the sense that the level of the basal [illegible]

[illegible] with the casual readings The fact that, when comparing one [illegible] within a comparable physiologic group, the casual blood pressure is to be regarded [illegible] of two independent variables has statistical implications. The supple- [illegible] among

Low Blood Pressure [illegible]

[illegible] to [illegible] m- [illegible] ilts [illegible] to develop [illegible] not neces- Poor vasomotor control and systolic blood pressure [illegible] sarily occur together The symptoms of persistent fatigue, dizziness and fainting

attacks are not due to persistent hypotension, being frequently found in association with normal or elevated blood pressure. These symptoms are frequently due to psychoneurosis.

It is notable in psychoneurotic patients who have blood pressure of 90 to 110 mm. that, at such times as the anxiety or other underlying emotional disturbance is less evident, not only are the general symptoms relieved but the blood pressure reading may be somewhat higher. Conversely, when the emotional disturbance again becomes prominent, the blood pressure may gradually fall to the lower levels.

Postural or orthostatic hypotension is characterized by the occurrence of faintness or loss of consciousness on rising from the recumbent to the erect posture In this disorder the blood pressure may fall sharply from normal or elevated levels in the recumbent position to pressures of the order of 40 to 50 mm systolic and 25 to 40 mm diastolic in the erect position with loss of consciousness. It is usually considered that postural hypotension is due to a failure of splanchnic vasoconstriction to offset the gravitational effects of the assumption of the erect posture.

Orthostatic Tachycardia and Orthostatic Hypotension. MacLean, Allen and Magath have divided orthostatic tachycardia and orthostatic hypotension into two groups: (1) inconsistent orthostatic failure of venous return and (2) consistent orthostatic failure of venous return

Inconsistent orthostatic failure of venous return is manifested by orthostatic weakness, faintness and occasional syncope associated with orthostatic hypotension or tachycardia, and an abnormal Flack reaction. The Flack reaction is characterized by increased intrathoracic pressure, the venous return fails to the extent that there are a marked decrease of the filling of the heart, decreased cardiac output and subsequent failure of the peripheral pulse. Both signs and symptoms disappear in the recumbent position Hypotension, if present, is associated usually with compensatory tachycardia There may be only tachycardia in the erect posture associated with occasional drops of blood pressure or diminished pulse pressure Both signs and symptoms are usually much worse in the morning after the patient first gets out of bed and quickly improve after the subject continues to maintain the erect state At times during the day an abnormal Flack reaction may be the only indication that the patient has a potential defect of venous return

Usually no objective evidence of an organic dysfunction of the autonomic nervous system can be demonstrated. The circulatory failure encountered in this inconsistent group appears to be associated with undue shifts of blood volumes and extracellular fluid, gravitating to the lower extremities The increased heart rates, low blood pressures and abnormal Flack reactions can be abolished by the assumption of the recumbent position or by the application of tourniquets around the thighs It has been the experience of these writers that the loss of volume of circulating blood through abdominal pooling appears to be a minor and relatively unimportant factor as compared with the loss related to the lower extremities

A normal man may exhibit at times the signs and symptoms of failure of venous return The margin between adequacy and incompetence is so narrow that when a man stands erect without moving he may be the subject of circulatory collapse Such failure may be precipitated by a variety of factors: exposure to heat, loss of blood, poor tone of striated muscle, psychic trauma or the maintenance of a recumbent state for overlong periods.

It is common to witness rapid heart rates and low blood pressures of patients who are allowed to stand for the first time after protracted rest in bed This postural instability is functional, in that it is reversible. If such a patient continues to stand erect for longer and longer periods each day, vascular stability is regained. The normal man can stand erect motionless for about one half hour (see Posture, Chapter 6)

Orthostatic hypotensive tendencies and orthostatic tachycardia are observed

commonly during gestation. Psychic syncope (fainting) seems to be largely postural and the cerebral ischemia can be prevented by the recumbent state. Some patients have constitutional defects of venous return which may be termed neurocirculatory asthenia. Occasionally the signs and symptoms of this disorder are orthostatic in origin and are characteristic of orthostatic failure of return of adequate amounts of venous blood to the heart

Caloric and rotational stimulation of the vestibules of normal man, varieties of seasickness and airsickness the symptoms of which are postural, undue exposure to heat, abnormal loss of body fluid and primary shock with its nervous basis of pain and psychic factors, all may demonstrate defects of venous return of varying degree which frequently play major roles in the total functional disability In these conditions the assumption of the erect posture may precipitate failure of venous return which is masked by the recumbent state

The pressure of hypertension is compatible with abnormalities of venous return Occasionally large drops in blood pressure of more than 100 mm. of mercury are observed when a patient who has hypertension first stands erect after a period of rest in bed Such changes of blood pressure are as a rule transient, lasting only a few seconds, but during this period the Flack reaction may be markedly positive, returning to normal when previous levels of blood pressure are established

Consistent orthostatic failure of venous return is manifested by severe orthostatic hypotension Objective evidences of disorders of the autonomic nervous system are common loss of sweating over large areas of the body surface associated with intolerance to heat, frequent absence of compensatory reflex tachycardia, and impotence Symptoms related to the deficit of venous return result from the erect posture or from application of a tourniquet to the femoral arteries of the legs. The Flack reaction is invariably positive, and frequently a deep inspiration will cause the peripheral pulse to disappear The signs and symptoms show classic exacerbation in the morning, which is related to rest in bed. Remissions are rare according to MacLean, Allen and Magath

Hypertension (Hyperpiesis) The term hypertension refers to a state of elevated blood pressure, both systolic and diastolic but frequently with only significant systolic increases, in a patient who does or does not have obvious or determinable organic changes in the tissues The condition may be attended with associated symptoms or may be asymptomatic If symptoms are present they may be associated with the primary disease—for instance, a glomerulonephritis—and not due to the hypertension

INCIDENCE. The frequency of hypertension increases steadily with age About one fifth of men between the ages of 20 and 29 years have readings of 140 mm systolic and 90 mm. diastolic or higher The greater degrees of hypertension are relatively infrequent at these ages, readings of 150 mm systolic and 100 mm. diastolic or more occur in only 1 of every 20 cases.

Hypertension of at least mild degree is common in middle-aged and old persons Blood pressures of 140 mm systolic and 90 mm. diastolic or higher are present in about 40 per cent of both men and women at ages 45 to 49 years, and in 60 per cent at ages 60 to 64 years Readings of 150 mm systolic and 100 mm diastolic or higher are found in nearly 20 per cent of persons by the age of 45 years Thereafter the incidence rises steadily to more than 35 per cent in both sexes between the ages of 60 and 64 years Whatever definition of hypertension is used, the condition is found more frequently in men than in women up to the age of 45 years. After that age the incidence is generally higher in women

Transient Hypertension. Levy, Hillman, Stroud and White made an analysis of the medical records of 22,741 officers of the United States Army in order to appraise the significance of *transient hypertension* Blood pressure readings higher than 150 mm. of mercury systolic or 90 diastolic were considered abnormally high

The length of the observation period was from 1 year to more than 25 years; 84 per cent were under observation from 5 to 19 years and 38 per cent from 15 to 19 years In 1,437 instances the duration of the observation period was 20 years or more

The frequency with which transient hypertension was first noted increased with age. The curve of increase was smooth, beginning with 5 9 per cent in the age group 25 to 29 years and reaching a plateau of 18.6 per cent at 50 to 54 years

At all ages, sustained hypertension developed more frequently in those with previous transient hypertension than in those who never showed an elevation of blood pressure. In both groups the rate increased with advancing years.

The rate for disability retirement of an officer who had cardiovascular-renal disease was consistently higher among those with transient hypertension than in those without, at all ages from 35 to 60 years

The death rate with cardiovascular-renal diseases was also higher in those with transient hypertension; the figures rose in the older age groups.

Hypertension and Endocrine Disorders. Hypertension occurs as a symptom of *endocrine disease,* and presumably results from hyperfunction of the thyroid and pituitary glands and from tumors of the medulla (paroxysmal hypertension) or cortex (Cushing's syndrome) of the suprarenal glands. In hyperthyroidism there is frequently a rise in systolic pressure and pulse pressure which is thought to be due to the increased general metabolism In cases of hyperfunctioning tumors of the suprarenal medulla, sometimes termed paragangliomas, the elevation of blood pressure usually, but not always, occurs in paroxysms There is evidence that the sudden, marked rises in blood pressure are due to the release of epinephrine or closely allied norepinephrine from the tumor.

Hypertension and Toxemia of Pregnancy. In the toxemia of pregnancy (eclampsia) hypertension is a prominent feature A similar type of hypertension is present in a condition which Keith and Wagener have designated as acute vasospastic disease with hypertension

A primary glomerulonephritis or an essential hypertension may exist before the onset of pregnancy and may undergo exacerbation in the course of the pregnancy with resultant toxemic manifestation, and these patients are best cared for if the primary renal or the primary vascular disease is recognized to exist along with the toxemia The patients in whom elevation of blood pressure occurs rapidly for the first time during pregnancy have a primary toxemia incident to pregnancy

Hofbauer has suggested that there may be a disturbed balance in certain hormonal regulatory mechanisms and homeostatic adjustments of normal gestation The various factors involved in the imbalance are to be seen in the hyperactivity of the pituitary, the adrenal cortex and the accessory medulla-like formation occurring in the cervical ganglia during gestation He has called attention particularly to the pronounced secretory

of the adrenal medulla The structure appears to act during the gestation as an accessory adrenal-medullary tissue functionally interrelated with the hypophysis, the adrenals, the ovaries and the placenta The histochemical appearance, in the pregnant state, of these pheochromocytes points to the increased formation of epinephrine, norepinephrine or allied substances The enhanced chromaffin activity of these ganglia has a stimulating effect on the anterior pituitary-adrenocortical system Certain physical factors in the second half of the gestation or during labor act mechanically to increase the release of epinephrine secreted by these cells into the circulation. In preeclampsia, Hofbauer points out, pronounced eosinopenia, sodium and chloride retention, increased urinary 17-ketosteroids and uric acid excretion afford sensitive indicators of anterior pituitary-adrenocortical stimulation, with the activation of secretion of pituitary adrenocorticotropic hormone most likely due to epinephrine

Hypertension and Arterial Degeneration. Atherosclerotic degenerative changes of both the larger and smaller arteries may cause an elevation of the systolic blood pressure but there is no increase in the diastolic blood pressure in the former.

Hypertension and Increased Intracranial Pressure. Increased intracranial pressure may cause a rise in systolic blood pressure (160-170 mm. Hg) but since such a mechanism is present for only a short time hypertension seems unlikely

Hypertension and Acute Vasospastic Disease. Wagener observed and described visible vasospastic changes in the retinal arterioles in those who have eclampsia He and others have observed the same condition of the retinal arterioles in men and in nonpregnant women. These patients have some of the symptoms of eclampsia. They have an acute onset of symptoms with a rapidly increasing blood pressure from its normal or elevated state prior to symptoms. These patients differ from those who have acute glomerulonephritis in that the evidence of renal damage is minimal or absent

Hypertension and Renal Disease. Patients who have acute glomerulonephritis often have hypertension which begins early in the disease This hypertension may persist or it may disappear when the glomerulonephritis heals. During this early period of hypertension and edema Keith observed that the fundi usually appear to be normal In an occasional instance, however, slight edema may be present about the disk margins and there may be present a few hemorrhages. These mild retinal changes and hypertension may be secondary to the general toxemia which caused the nephritis, including the fever

In those who have more severe acute nephritis, improvement of the hypertension, if present, and general improvement, as indicated by the disappearance of edema, come slowly. In these patients there usually develop chronic glomerulonephritis attended by a retinitis Some of them will have hypertension and some will not The retinitis develops as a result of edema, anemia and angiospasm. The patients who have both persistent moderate hypertension and generalized edema may have edema in the retina without fully developed retinitis.

In those who have chronic glomerulonephritis with a minimal increase in blood pressure or perhaps no hypertension and in whom there is anemia of severe degree, hemorrhages and cotton-wool exudates may appear in the retina without angiospastic accompaniments Such a retinitis cannot be distinguished in general from that seen in anemia from any other cause However, if the blood pressure is due to chronic nephritis, the presence of persistent narrowing of the retinal arterioles may help to distinguish the retinitis from that which occurs in primary anemias

Angiospastic retinitis characterized by edema of the disks, diffuse edema of the retina, exudates of a cotton-wool appearance, hemorrhages, star-shaped macular lesions and visible sclerotic changes in the arterioles may be present in patients who have chronic glomerulonephritis with complicating or associated diffuse arteriolar disease and hypertension These retinal findings indicate that a diffuse arteriolar disease has preceded the onset of glomerulonephritis

These angiospastic and sclerotic lesions in the retinal arterioles indicate that thenceforward the vascular manifestations, including the hypertension, will assume the dominant role in the progress of the disease.

Essential Hypertension. The cause of essential hypertension has not been assigned. The consensus is that abnormal physiologic processes which may give rise to hypertension comprise four factors: (1) increased cardiac output, (2) increased viscosity of the blood, (3) increased total blood volume and (4) increased resistance in the peripheral circulation. Increased cardiac output may be responsible for the hypertension found in some cases of aortic insufficiency and in patients with arteriovenous fistula However, in most instances of essential hypertension the cardiac output is normal. The viscosity and the total volume of the blood are in-

creased in polycythemia vera, whereas the blood pressure is normal or only slightly increased.

An increased *peripheral resistance,* that is, a resistance in the arterioles or capillaries, seems to be a prime factor in the production of the measurable arterial hypertension. This contention is based on histologic examination which reveals changes in the medial walls of peripheral arterioles throughout the body These changes consist of medial thickening which reduces the size of the lumina of the vessels A reduction in size of the lumina of these small vessels could give an increased resistance to the blood flow. As soon as the postulation is made that there are present increased peripheral resistance and arteriolar changes sufficient to cause an increase in blood pressure, there is no way to answer which came first, the peripheral resistance or the arteriolar changes

Goldblatt's experiments on the production of renal ischemia in animals have revived interest in the old question of the relation of renal disease to diffuse arteriolar disease and hypertension. The observation that hypertension will still develop in the ischemic kidney after the destruction of the nerve supply of the kidney indicates that there may be present an active hormone having its origin in the kidney and set free into the general circulation and that it is this substance which causes hypertension The nature of such a circulative substance and its mode of action are unknown. Prior to Goldblatt's experiments, Tigerstedt and Bergman demonstrated that a simple saline extract of the fresh renal cortex of normal rabbits contained a pressor substance which they called renin. This substance was not obtained from any tissues of the experimental animals other than renal tissues The site of action of renin appears to be in the peripheral arterioles

hypertension In the early period of essential hypertension in man there is no renal insufficiency.

Weitz observed the evidence of heredity in hypertension by measuring the blood pressure of brothers and sisters of hypertensive persons and found that the incidence of elevated blood pressure was significantly greater among siblings of persons with hypertension than among siblings of persons without hypertension. Ayman studied the blood pressure of every member of a family for three generations, totaling 32 members more than 13 years of age One hundred per cent of the first generation, 80 per cent of the second and 25 per cent of the third had elevated levels of the blood pressure on two or more readings Ayman in a later article reported on a direct study of the blood pressure, height and weight of 1,524 members of 277 families Elevated systolic and diastolic blood pressure readings occurred in 148 of 780 members of the second generation aged from 14 to 39 years These 148 subjects had the same average age and sex incidence as the entire group of 780 children, but they were 14⅓ pounds (6 5 kg) above the average weight compared to 4½ pounds (2 kg) above the average weight for the remainder of the group In families whose parents had absolutely normal blood pressures the incidence of elevated blood pressure in the children was only 3.1 per cent In families in which one parent had arteriolar hypertension the incidence of elevated readings in the children rose to 28.3 per cent In the families in which both parents had arteriolar hypertension the incidence of elevated readings in the children reached the level of 45 5 per cent Of 70 brothers and sisters of parents whose blood pressure was normal, 37 3 per cent had elevated blood pressure readings, whereas of 86 brothers and sisters of pa[illegible]

pressure rea

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as compared with similar relatives of subjects with normal blood pressure, offers strong evidence for the existence of a hereditary factor in the etiology of hypertension.

Faulty diets have been associated with, and assigned as a cause for, hypertension in some patients The responsible factors in or absent from the diet have not been determined

The group predisposed toward hypertension on a hereditary basis must frequently acquire faulty dietary habits, as habits of food selection are handed down through families with little change from one generation to the next The effect of diet and overweight is also well demonstrated by the benefit incident to correction of these factors in patients in whom hypertension has developed

Increased blood pressure is produced by *anger and fear*. Stimulation of the sympathetic nervous system in anger and fear by an increased amount of norepinephrine and epinephrine in the blood stream causes rise in blood pressure The repression of chronic fear or chronic rage according to the psychiatrist eventually manifests itself in the circulatory system by the production of a continuous state of increased tension through the mechanism of sympathetic nerves, and norepinephrine and epinephrine-induced generalized vasoconstriction

Long-continued increased tension eventually produces degenerative changes in the intima and thickening of the walls of the arterioles Although these changes frequently occur as one of the degenerative changes of increased age, they are apparently greatly speeded by hypertensive states Changes are generalized and include the afferent renal vessels.

It has been suggested that hypertension is due to abnormal development of arteriovenous fistulas such as normally exist in the tips of the fingers and toes and in certain parts of the kidneys There is little evidence to support this hypothesis.

Hines and Brown, interested in the vasomotor factors in hypertension, devised a standard test for measuring the maximal vasomotor response when the hand and arm were immersed in cold water Individuals who have essential hypertension show a much greater increase in pressures with the cold water test than those who do not have essential hypertension Among patients who had early or "preorganic" hypertension, the average increase of blood pressure was 34 mm. of mercury systolic and 25 mm diastolic Among the patients who had an "organic" stage of essential hypertension, the average increase of blood pressure was 47 mm of mercury systolic and 34 mm diastolic

As a result of a study of 190 members of 15 family groups, 6 without and 9 with definite evidence or history of hypertension, Hines and Brown expressed the opinion that the vasomotor reaction to cold follows an inherited pattern and that the excessive or hypertensive type of reaction occurs in the families in which there is a hypertensive diathesis. They were led to believe that "the abnormality of essential hypertension is an excessive response in the blood pressure to intrinsic and extrinsic stimulation. This hyperreactive vasomotor mechanism may be an important factor in the production of arteriolar hypertrophy and in the subsequent development of the organic stages of the disease."

Hines and Brown found that the systolic form of hypertension seen in cases of senile arteriosclerosis and in cases of glomerulonephritis gave definitely less response to the cold pressor test than did the pre-existent and existent stages of essential hypertension

For a long time comments have been made in regard to the temperament which was apparent early in the life of hypertensive patients. These children are tense and more conscientious than the average child of their age. On examination of such a child there is present evidence indicating vasomotor weakness such as frequent epistaxis; excessive menstruation, cold, sweaty and cyanotic hands, flushing; blinking of the eyes and other evidences of a high-strung temperament.

PATHOLOGY Barker has summarized the pathologic changes in hypertension as consisting primarily of the development of a spastic thickening of the walls of the arterioles throughout the body which gradually becomes organic The secondary manifestations are myocardial weakness and failure as the result of increased myocardial strain, and the premature development of degenerative changes in the large arteries, also as the result of strain The degenerative changes in the larger arteries occasionally result in rupture, more commonly in thrombosis, and either of these events may be serious or fatal if the vascular accident occurs in a vital organ such as the heart or brain Serious lesions of the kidneys may occur as the results of chronic ischemia in hypertensive patients. When death occurs, it is most commonly the result of myocardial failure, second most commonly the result of cerebral vascular accidents and third most commonly the result of renal insufficiency.

CLASSIFICATION OF ESSENTIAL HYPERTENSION. The most widely known classification of essential hypertension is Volhard's red and pale hypertension Keith and Wagener admit the merits of Volhard's basic conception of these two conditions, but they are convinced that it is more appropriate to classify hypertension on the evidence of the differences in the arteriolar changes. In support of the soundness of their classification, which is based on changes in the retinas, they took biopsy specimens from striated muscle and found a close correlation between arteriolar changes in the muscle and those revealed on ophthalmoscopic examination Muscles were selected for the purposes of biopsy because this tissue represents one of the large bulky systems of the body.

Their histologic study of biopsied muscle disclosed that in some cases the arterioles appeared to be normal, whereas, in many others the walls of the arterioles were thickened, the ratio of the diameter of the lumen to the thickness of the wall was definitely decreased In many instances this change was uniform for all the arterioles seen In some it was confined to the smallest arterioles, and in others there were marked variations and localized changes only Other changes consisted of increased prominence and tortuosity of the arterioles and an increase in the number and size of medial and intimal nuclei Occasionally there were organized thrombi, extensive intimal proliferation, complete occlusion of the lumen by simple hypertrophy of the media, and perivascular collections of lymphocytes and fibroblasts Medial necrosis was found in the arterioles of voluntary muscle as well as in those of the kidneys and other organs in malignant hypertension. None of these changes were found in the histologic sections of muscles of persons with normal blood pressure. Similar findings to those found in the arterioles of striated muscle were demonstrated in the arterioles of the retina

Keith and Wagener's classification of essential hypertension is based on the foregoing studies which emphasize the widespread dissemination of the arteriolar

sion the patient is assigned The division of hypertension into four groups by these observers is based on the following criteria.

Diffuse Arteriolar Disease with Hypertension, Group 1. These patients are usually between 20 and 55 years of age Members of this group constitute the great majority of those who have hypertension, and they often have good health for years.

The evidence of the hypertension often is first found at the time of routine examination Prior to such an examination there have been no symptoms There are no symptoms in the stoic individuals after they know the blood pressure is increased It is different in the psychoneurotic individuals, who often become hypertensive hypochondriacs.

On examination there may or may not be obesity. The blood pressure is 150 to 175 mm. of mercury systolic, 90 to 95 mm of mercury diastolic. Often the diastolic

pressure is normal The heart is not enlarged or seemingly abnormal in any way. When the radial artery is made pulseless at the wrist by compression at the elbow, the pulseless artery may or may not be palpated. If it should be palpable, it imparts the sensation of a soft, collapsible tube to the palpating finger.

Twenty-four-hour studies of blood pressure demonstrate the decidedly beneficial effect of rest on the hypertension. During rest and sleep the blood pressure is often within normal limits and the retinal changes are usually minimal and consist of mild narrowing or mild sclerosis of the arterioles. Spasm of the arterioles is not present

The changes in the arterioles of the muscles likewise are minimal. Examination of the urine reveals no abnormality, or at most the urine contains albumin grade 1 on a basis of 1 to 4, in which 1 indicates the least amount of albumin and 4 the greatest amount More than albumin grade 1 arouses the suspicion of a previous nephritis The urinary sediment is negative

Diffuse Arteriolar Disease with Hypertension, Group 2 These patients, like those of group 1, vary in age from about 20 to 55 or more years They may be obese

If these patients are ill, it is not from their hypertension However, the blood pressure is distinctly elevated, 160 to 185 or more systolic and 90 to 100 or more diastolic Some of the patients may have headaches. Nocturia is often present, particularly in the aging patients The heart may or may not be enlarged Obliteration of the radial pulse by pressure at the elbow reveals a definitely palpable thickened radial artery at the wrist Often flexion of the elbow will reveal that the arteries of the arm have lost a considerable part of their elasticity and do not contract with the flexed arm. They seem to be too long and are observed to be tortuous tubes pulsating in two planes

There is usually a response to rest by the blood pressure, perhaps a return to normal values will be revealed while the patient is asleep

Patients of this group have continuously a higher blood pressure than normal and more distinct changes in their retinal arterioles The arteriolar sclerosis is often graded 2 to 3 on a basis of 1 to 4 There is no, or at most minimal, angiospasm

Histologic studies of the muscle arterioles disclose a more uniform and more marked narrowing than is evident in the arterioles of group 1. In addition to narrowing of the lumen of the vessel, there may be thrombosis or occlusion of arterioles.

The urine usually contains albumin grade 1 to 2. The urinary sediment often contains hyaline and granular casts but rarely microscopic blood

As these patients pass into the aged groups of individuals, atherosclerosis is often superimposed, and any one of the cerebral, cardiac or renal accidents incident to this disease may occur The impression is gained that a person who has arteriosclerosis with hypertension is more susceptible to atherosclerosis than one who does not have arteriosclerosis

The clinical impression is gained that the patients of group 2 have a progressive disease. The hypertension of patients in group 2 more nearly corresponds to Volhard's designation of red hypertension

Diffuse Arteriolar Disease with Hypertension, Group 3. These patients are between 20 and 55 years of age, and men are more commonly affected than women

Generally there are headaches, feelings of fullness in the head, failures of vision, nosebleed, dizziness and unsteadiness of gait Often there is exertional dyspnea, cough, or other symptoms of left-sided heart failure. Nocturia and polyuria are common All of these symptoms may increase rapidly, then remain stationary for a time and then regress, but more often they tend to progress and increase in intensity

On examination these patients often have a general pallor, the so-called pale hypertensives of Volhard. There is often evidence of loss of weight. The blood pressure is high; 200 to 300 mm. of mercury systolic and 100 to 130 mm. or more diastolic are common. The radial arteries, however, may not reveal much arterio-

sclerosis. Often the sclerosis is not more than grade 2 on a basis of 1 to 4 The pulse rate is often increased. The heart is enlarged and the aortic second sound is accentuated Basal aortic systolic murmurs are common Edema of the ankles may be present after the patient has been on the feet for an hour or two The urine contains albumin, and often the presence of blood and a few casts may be revealed by microscopic examination. The concentration of urea nitrogen in the blood may be increased, depending on the degree of renal involvement More often there is present an inability of the kidneys to concentrate urine. The specific gravity of the urine has a limited range of variability (1 010 to 1,015).

An important criterion is the presence of angiospastic retinitis, together with definite sclerotic changes in the arterioles but no edema of the disks. In those who have had a remission from the progress of the disease there may be evidence in the retina of previously active retinitis, indicated by the obliteration of small arterioles. In such cases small arterioles of the retina undergo thrombosis, and a similar process may have occurred in the skeletal muscles.

On examination of the arterioles of the skeletal muscles, the lumina of the arterioles are decreased in size; definite cellular lesions and thrombosis are often present.

Diffuse Arteriolar Disease with Hypertension, Group 4 (Malignant Hypertension) This disease affects men more frequently than women The onset often occurs between the ages of 20 and 55 years Malignant hypertension has been reported, however, in older individuals and in children.

These patients are nervous, tense and weak and complain of visual disturbances or, more likely, faulty vision or definite failures of vision Headaches are often intense, and may approach in severity those caused from intracranial hypertension.

Dyspnea, palpitation, and some enlargement of the heart are often present The radial artery may be sclerosed, grade 2 or 3 on a basis of 1 to 4 Blood pressures range from 200 systolic upward measured in millimeters of mercury, and the diastolic may be 130 to 140

The urine contains albumin and often blood. In an occasional instance there may be profuse renal hemorrhages which are sufficient for blood clots to form in the ureters and cause acute colic. These clots are usually expelled spontaneously

The important retinal alterations are the marked spastic and organic narrowing of the arterioles with diffuse retinitis and edema of the disks The edema of the disks, if accompanied by the severe headaches, may require differentiation from increased intracranial hypertension

The arterioles of muscle obtained by biopsy reveal great narrowing of the lumina, cellular lesions and often thrombosis or occlusion

The prognosis is serious, only one of Wagener and Keith's patients lived as long as 40 months. Seventy-nine per cent were dead within a year However, one patient was alive 11 years after the first observation

Not in all cases of group 4 is the course so rapid Some patients even have periods with subsidence of the retinitis and with clinical symptoms which suggest remission Such cases belonging to group 3 were considered previously. Here again in group 4 spasm of the arterioles may determine whether the condition is progressive

Differentiation of Groups. The numbers 1 to 4 were employed by Wagener and Keith to avoid confusing terminologies The numbers 1 to 4 do not imply a progression from 1 to 4 in all instances of hypertension The number used designates or classifies the group of hypertension to which the patient belongs at the time of the first examination In reality, a patient belonging to group 1 may suddenly become a member of group 4, or a patient belonging to group 3 may become a member of group 1 and in very rare instances one who has hypertension group 4 may have a remission in the retinal findings and be classified as belonging to group 3.

Clinical differentiation of the four groups of essential hypertension, one group from another, may not be accomplished without difficulty. Patients of groups 1 and 2 have good retinal, cerebral, cardiac and renal function, whether the hypertension be labile, or high, with a tendency toward fixation In those belonging to group 3 there is evidence of dysfunction of one or several of the organs belonging to the arterial system, while in group 4 these functional disturbances become more effective and final failure may occur because of a simultaneous serious interference in the blood supply to the retina, brain, heart and kidneys. Difficulties of differentiation of one group from another arise when in a given case the disease progresses rapidly so that the patient passes from group 1 to group 4 in a short period

Examination of the ocular fundi is of considerable aid in determining the group in which an individual patient with hypertension belongs For practical clinical purposes those who have only purely organic changes in the arterioles of the retina belong to group 1 or group 2, while patients who show definite evidence of angiospasm belong in group 3 or group 4.

Thrombosis of the retinal veins is considered to arise either on the basis of organic changes alone or as the result of an infectious process (phlebitis) superimposed on a mild organic lesion Patients who have retinal venous thrombosis usually belong in group 2, although the other clinical and laboratory findings at times may justify their classification with hypertension of group 3 Cases of retinitis of arteriosclerosis usually can be placed in group 2 unless the retinitis can be shown definitely to be the residuum of a previously angiospastic type of retinitis.

Patients who have retinitis of angiospastic type, characterized by edema, cotton-wool-appearing exudates, and hemorrhages in the retina superimposed on a combination of sclerotic and spastic lesions in the arterioles, belong to hypertension group 3 or group 4. Patients who have cotton-wool-appearing exudates and hemorrhagic areas in the retina, but whose optic disks are not edematous, usually belong to group 3 The most characteristic feature of the disease in cases of hypertension of group 4 is measurable edema of the optic disks, which usually occurs, of course, in association with the other features of widespread angiospastic retinitis and in intracranial hypertension

Acute angiospastic retinitis is a part of vasospastic disease which is often present in the toxemias of pregnancy and active severe arteriolar sclerosis The ophthalmoscopic findings in these conditions vary from those of localized areas of edema of the retina, with cotton-wool-appearing exudates and hemorrhages, to that of retinitis, with diffuse edema of the retina In both acute angiospastic disease and toxemia of pregnancy, the retinitis may completely disappear under favorable circumstances, leaving as residuals varying grades of sclerosis of the retinal arterioles, depending on the severity and persistence of the underlying angiospasm. The features of an angiospastic disease which may clear up depend on the presence of angiospasm, generalized and localized irregular narrowing of the arterioles, and absence of organic changes in the vessel walls, such as visible thickening of the wall, exaggerated reflexes and arteriovenous compression. In an angiospastic disease when organic changes are developing in the walls of the arterioles, differentiation of group 3 or group 4 may be difficult or impossible without the presence of edema of the disks as regularly occurs in group 4

Wagener and Keith have expressed the belief that in the beginning of a toxemia of pregnancy the differentiation between retinitis of hypertension and "albuminuric retinitis" (nephritis) cannot be made except by the time element, since in most patients who show primarily a few cotton-wool patches and hemorrhages the characteristic appearance of albuminuric retinitis will later develop unless the pregnancy is terminated spontaneously or otherwise In the pregnant woman, as in the non-pregnant woman, the albuminuric type of retinitis is more often the result of diffuse arteriolar disease than it is of primary glomerulonephritis

organic changes in the vessel walls. However, they have observed that permanent organic changes at times may take place in the arteriolar walls after persistent spasm without the development of retinitis.

PROGNOSIS Many of those who belong to groups 1 and 2 live their normal life expectancy However, these patients often pass on to middle or old age, and then atherosclerosis develops, and thus heart failure, renal failure or strokes ensue

The prognosis for patients in group 3 and especially for patients in group 4 is grave. A death rate within one year of one third of those in group 3 and about two thirds of those in group 4 is in distinct contrast to that of 1 of every 10 in groups 1 and 2.

The prognosis in a group of patients who have hypertension from various causes has been forecast by Frant and Groen who reported a follow-up of 418 patients with hypertension (blood pressures above 155 systolic and 100 diastolic) who were re-examined after a period of 8 to 9 years. The death rate for men with essential hypertension exceeded the normally expected death rate in the same age groups by 102 per cent, for the women this figure was 91 per cent Chronic nephritis increased the death rate in men by 587 per cent and in women by 150 per cent. Hypertension related to toxemia of pregnancy carried a mortality of 155 per cent in excess of the normal The total excess mortality for patients with hypertension of all types was 233 per cent for the men and 201 per cent for the women The mortality increased with increase of both systolic and diastolic blood pressure.

The condition of the fundus of the eye is a better guide for the prognosis of hypertension than the increase in blood pressure. In the cases studied by Frant and Groen heart disease, albuminuria and diabetes appeared to reduce the expectation of life even more for women than for men Hypertension accompanied with obesity appeared to be prognostically more favorable than the same hypertension in patients whose weight was normal or low Hypertension in young subjects carries a relatively shorter life expectancy than high blood pressure in old age Heart disease is first among the causes of death of patients with hypertension, it accounts for 40.9 per cent, next comes carcinoma (16.4 per cent), followed by uremia (14 9 per cent) and apoplexy (8.6 per cent) Apoplexy as cause of death was almost five times as common among women (14.2 per cent) as among men (3 1 per cent). The cause of death could not be ascertained for 9 4 per cent

The prognosis seems to be better since the advent of new drugs.

Arteriosclerosis and Atherosclerosis With and Without Hypertension. Hypertension with an increase in diastolic pressure is probably not present without disease of the smaller arteries or arterioles Indeed on general examination there may be evidence present of disease of the larger and smaller arteries without an accompanying hypertension Determination of the basal blood pressure reveals a pressure within the limits of normal for the age group to which the patient belongs However, these observations, if made in the presence of manifest cardiac or renal disease, may be diagnostically misleading, for such patients may have had a very low normal basal pressure prior to the development of manifestations of cardiac or renal disease Such observations require definitions of arteriosclerosis, arteriolar sclerosis and atherosclerosis

Definitions of arteriosclerosis, arteriolar sclerosis and atherosclerosis are difficult, for these terms have been variously employed to mean different forms and degrees of vascular disease as well as the same vascular disease

The term arteriosclerosis (hardening of the arteries) in its broad use refers to degenerative vascular changes which are not due to syphilis, rheumatic fever or specific infectious diseases, and the term does not include the conditions known as thromboangii-

tis obliterans, periarteritis nodosa and lupus erythematosus. Arteriosclerosis designates a condition marked by loss of elasticity, thickening and hardening of the arteries. Appropriate adjectives designate the region of the body most profoundly affected, for instance, cerebral, coronary, or in the case of widespread disease, general arteriosclerosis. A special form in medium-sized and smaller-sized arteries characterized by a primary necrosis and calcification of the medial coat is termed Monckeberg's sclerosis.

As the term arteriolar sclerosis commonly is used, it designates changes in the *smaller arteries* and *arterioles* which are characterized by endothelial hyperplasia, thickening and hyalinization of the intima and hypertrophy of the media of the arterioles of the kidneys and other viscera, and which are more uniformly distributed in the arterioles than is either arteriosclerosis or atherosclerosis in the larger arteries. Arteriolar sclerosis is always associated with hypertension. These arteriolar changes are of the type of vascular disease responsible for essential hypertension (groups 1 to 4) of Wagener and Keith.

Atherosclerosis affects the *large* and *medium-sized arteries,* such as the aorta and the coronary and cerebral vessels, the arteries to the arms and legs, and the larger peripheral arteries. The condition is characterized by intimal thickening due to lipoid atheroma, fibrosis, calcification, necrosis and hemorrhage. This is the type of arteriosclerosis which involves the coronary and cerebral arteries and is often responsible for arteriosclerotic heart disease and cerebral apoplexy in those who do not have hypertension.

Atherosclerosis is common after the age of 40 years. There is an increasing frequency with subsequent decades.

Heart disease, renal disease and cerebral disease due to arteriosclerosis and atherosclerosis are much more frequent among men than among women.

Hypertension is present in about one half of all the men and in about three fourths of all the women who have these degenerative forms of heart disease. Arteriosclerotic heart disease in the absence of hypertension suggests that hypertension is an aggravating factor and not the cause.

Arteriosclerotic heart disease develops with unusually high frequency among diabetic patients and those who have familial xanthomatosis with hypercholesterolemia, myxedema, or chronic glomerulonephritis and obesity.

The theories of the etiology of arteriosclerosis and atherosclerosis are concerned primarily with whether or not the disease is a process of aging or with conditions incident thereto such as metabolic disorders, inherited or acquired.

The life span of man no doubt does change according to various and unknown conditions arising within his own body or as the result of environmental conditions. It would be well to wait, before conclusions are drawn concerning the increasing span of human life as well as the purported increase in the incidence of arteriosclerosis and hypertension, to see whether these might not be just passing phases in the evolution of the species. To gloat over any particular achievements of this generation over the immediately former generations might prove to be premature.

In a similar vein the tempo of modern industrialized civilization is indicted as the cause of hypertension and hardening of the arteries. A comparison of the tempo and the emotional tensions of men who lived 25,000 or more years ago is not available. If such were available, might it not be just possible that these men and women had many tensions unknown to us now? Did they not have arteriosclerosis and hypertension often resulting in sudden death? One can be sure that if they did have angina pectoris or strokes, they were not accorded protection in bed for prolonged periods of time. The prolongation of such a life by bed rest alone is hardly worthy of praise as a medical accomplishment.

Transient, and occasionally permanent, hypertension may follow repeated, powerful emotional experiences involving fear, anxiety and hostility. A characteristic hypertensive personality and a distinctive psychiatric pattern have been described.

Hypertension is slightly commoner in women than in men. Hypertensive (and arteriosclerotic) heart disease is much more frequent in men.

GENETICS AND ATHEROSCLEROSIS Adlersberg, Parets and Boas have recorded 35 families with xanthoma and the relationship of this condition to hypercholesterolemia, coronary artery disease and related stigmas It appeared to these authors that a common factor for some patients with coronary atherosclerosis may be a hereditary disturbance of cholesterol metabolism manifested by elevated serum cholesterol. Familial xanthomatosis is the severest form of the inherited disturbance. Xanthomatous lesions develop only in patients who carry two abnormal genes for cholesterol, that is, they are homozygotes. Atherosclerosis is frequent in such persons. These authors believe as others do that some patients with uncomplicated coronary artery disease are probably affected with a mild form of disturbed lipid metabolism. They carry one abnormal gene for cholesterol; that is, they are heterozygotes Derangement of cholesterol metabolism helps explain the familial incidence of coronary artery disease and also accounts in part for its development in many persons less than 50 years of age.

METABOLISM The only constant factor in all the metabolic theories of arteriosclerosis is that cholesterol and other lipids play a common role in the production of the disease It is thought that the initial disturbance in atherosclerosis is one of solution or dispersion of cholesterol in the blood, due either to hypercholesterolemia or to alteration in other substances in the blood which diminish the solubility of cholesterol.

There are large amounts of cholesterol esters and free cholesterol in atheromatous lesions. The quantity present exceeds that which could be formed by local degeneration The concentrations of lipids in these lesions correspond to their concentration in the plasma.

Gofman and associates have pointed out that it is not the total plasma cholesterol which correlates with vascular sclerosis, but rather the presence and quantity of an abnormal cholesterol-containing lipoprotein

Since dietary cholesterol occurs in foods of animal origin with particularly desirable nutritional value (for example, meat, eggs and milk), it seems unwise on the bases of the present evidence to condemn use of these foods if there is risk of sacrificing the foundations of sound nutrition This is particularly significant and in accord with the observations of Keys and associates who observed that the serum cholesterol level of "normal" men is not significantly related to differences in the habitual cholesterol intake over a range of something like 250 to 800 mg per day.

Premature atherosclerosis occurs in diabetes However, the specific metabolic or endocrine factor in diabetes which predisposes to atherosclerosis is uncertain

OBESITY AND ATHEROSCLEROSIS Faber and Lund studied 408 aortas from necropsy material in hospitals and the medicolegal institute of Copenhagen. Two hundred and ninety-five of the 408 patients, 240 men and 168 women, from whom the aortas were obtained had been of normal weight and 113 had been obese Two hundred and eighteen of normal weight and 41 obese persons had had normal blood pressure, 77 of normal weight and 72 obese persons had had hypertension The great increase in the degree of sclerosis with rising age makes it necessary to eliminate the age factor from the evaluation of the sclerosis. The logarithm of the cholesterol and calcium content of the vessel wall and the dry weight of the tissue rises rectilinearly with age To eliminate the factor of age the formula for this line had been calculated for these three factors. Distribution curves for the dry weight, the total cholesterol content and the calcium content of the intima and media of the aorta around the calculated normal line for the four groups of persons studied [illegible] Comparison of these [illegible] bove what should be [illegible] of the factors studied when the presence of hypertension is taken into account

MANIFESTATIONS The manifestations of arteriosclerosis or atherosclerosis de-

pend on the individual arteries affected and their distribution to various members, organs or systems of the body. These symptoms are discussed in association with the organs or systems affected.

Symptoms arise when there is interference with the blood supply to the part caused by occlusion, partial or complete, or rupture of the artery Associated or unassociated with partial or complete occlusion or rupture of an artery, may be disturbances in conduction and rhythm of the heart, in cerebral functions, in digestive functions, and in locomotion attributable to atherosclerosis.

On examination either arteriosclerosis or atherosclerosis may be found without the demonstrable presence of the other. Arteriosclerosis often will be accompanied by hypertension Arteriolar sclerosis will always be accompanied by hypertension These conditions are diagnosed by ophthalmoscopic examination.

Examination when the arm is flexed at the elbow reveals a visible tortuous brachial artery which pulsates in two planes, for the artery has lost its elasticity. Often palpation of such an artery reveals small, hard, irregular plaques. The pulsations in such arteries, especially when those of the legs are involved, may reveal decreased or absent pulses

The roentgenograms often reveal the presence of radiopaque material along the course of the larger arteries in all parts of the body, especially the aorta, and the *pelvic vessels.*

The diagnosis of arteriosclerosis and atherosclerosis depends on the symptoms and physical signs resulting from the diminishing or the discontinuing of blood flow to the affected part

The peripheral arteries can be palpated, and often calcification in their walls can be demonstrated by roentgenologic examination

The presence of arteriosclerosis in a youth suggests the possibility that diabetes mellitus is present

Angina Pectoris. The immediate cause of angina pectoris is insufficiency of the coronary circulation

The causes of insufficiency of the coronary circulation, as enumerated by White, are (1) diseases of the coronary arteries due to atherosclerosis, infection, thrombosis or embolism, (2) the coronary arteries may be blocked at their mouths, partially or completely, by swelling and inflammatory reaction of the aortic wall in syphilitic aortitis, or by vegetations on the aortic intima or extending up from the aortic valve cusps in bacterial endocarditis There may be (3) marked aortic regurgitation with very low diastolic blood pressure, it is an ample diastolic blood pressure that normally maintains an efficient coronary circulation, for during systole the coronary arteries are compressed. There may be (4) marked aortic stenosis with low pulse pressure and limited output per beat which, doubtless with the added effect of suction by the forceful narrow jet of blood directed up the aorta with each heart beat, cuts down the coronary circulation There may be (5) severe anemia, pernicious or secondary, with insufficient oxygen in the blood carried to an active myocardium, even though the coronary arteries themselves are fairly normal There may be (6) too great a demand on the heart muscle, as in excessive exertion or thyrotoxicosis, so that the coronary circulation, though adequate at rest, is unable to maintain a sufficient blood flow to the myocardium under these circumstances There may be (7) spasm of the coronary arteries lasting a few minutes at a time in patients who have relatively normal vessels

Hypotheses of Pain in the Heart. There are two often quoted hypotheses of the origin of cardiac pain ischemia of heart muscles, and tension on the coronary arteries The following paragraphs summarize the observations of Blumgart on the origin of cardiac pain due to ischemia.

Ischemia. In the syndromes of angina pectoris, coronary failure and acute myocardial infarction, cardiac pain is an expression of a relative disproportion between the demands of the myocardium for blood and the decreased supply it receives through the coronary arteries The changes in the myocardium resulting from this disproportion depend on the duration of the ischemia If the ischemia is brief, the pain is brief, as in

angina pectoris, and no permanent myocardial damage may occur. If the ischemia is more prolonged, the pain is more severe and prolonged. If the duration of complete obstruction is longer than 15 minutes, irreversible changes, that is, myocardial necrosis, are produced, notwithstanding re-establishment of normal blood supply. When the blood supply has been interrupted for 40 to 45 minutes, widespread myocardial infarction is witnessed during the succeeding days, even though blood flow through the coronary arteries is not obstructed.

Cardiac pain is precipitated by effort, emotion and other states which increase the work of the heart, and is relieved by rest and other measures which lessen the work of the heart. Cardiac pain may be induced by breathing low concentrations of oxygen. All of these facts support the concept that cardiac pain is due to ischemia. The structural changes in the coronary arteries and in the myocardium must not be considered the exclusive cause of cardiac pain, but rather as constituting the stage on which various factors may operate. Thus vasoconstriction or absence of vasodilatation, effort, anemia, tachycardia or shock with its lowered blood pressure may act as precipitating agents in the production of pain in a heart whose circulation is already compromised by arterial obstruction.

Tension. According to Gorham the arguments for the tension hypothesis of cardiac pain have been advanced and supported by such evidence as the occurrence of coronary occlusion without pain. Pain is more frequent in the presence of acute fresh thrombosis and infarction and is less frequently encountered in old fibrous infarcts without actual thrombosis.

Pain is known to arise from blood vessels, owing to tension on the walls of arteries in instances of embolism of the peripheral arteries, in dissecting aneurysm and in migraine.

Tension is the commonest cause of pain, as noted in inflammatory lesions and in the colics produced by smooth muscle contraction in hollow organs.

Pain may be produced in the human heart affected with coronary sclerosis and the anginal syndrome by the injection of epinephrine.

Angina pectoris occurs predominantly in men. The disease occurs in women usually in association with diabetes or hypertension. The average age of onset is 56 years for men and 58 years for women.

There are no convincing data to prove that angina pectoris affects particularly those whose work subjects them to continuous mental tension. Angina pectoris occurs in individuals of all races and all social and economic strata.

The genealogic history often discloses that the patient's progenitors, in one or more lines of the family, suffered from angina pectoris. Of the affected line or lines of the family, the members who have angina pectoris are usually short and stocky, overweight, short-necked with barrel-shaped thorax.

These patients are aggressive, ambitious, serious-minded persons who possess deep emotional reactions.

PATHOLOGY. The pathologic changes are varied. They are those of any disease or condition which causes a narrowing and occlusion of the lumina of the coronary arteries. Diseases and states causing coronary narrowing are atherosclerosis, syphilitic aortitis, aortic valvular disease, reduction in aortic blood pressure, pulmonary embolism, shock states, reduction in oxygen content of the blood as in anemia, and arterial anoxemia, as caused by pulmonary or congenital heart disease, low atmospheric oxygen tension, and drugs.

SYMPTOMS. Angina pectoris is characterized by paroxysmal attacks of pain or oppression, situated retrosternally, and extending commonly to the precordium and left pectoral girdle, usually to the arm.

The pain in angina pectoris is as a rule dull and throbbing, is produced by effort, and is relieved immediately by rest or nitrites. The pain of acute myocardial [illegible]

[illegible] nged

[illegible] the

syndrome. The pain of angina pectoris rarely occurs while the patient is at rest

In such a patient, if the pain or oppression cannot be reproduced by exertion or sexual intercourse, the diagnosis of angina pectoris is dubious

The pain during a paroxysm of angina pectoris is usually situated at or behind the middle or upper third of the sternum, centered at the level of the third or fourth rib. Occasionally the pain is more extensive and covers most of the precordium A pain that is situated at or near the cardiac apex or to the left of the cardiac region is not due to angina pectoris

The pain of angina pectoris, when it is severe, tends to extend to the arm, neck, and occasionally to the jaw. In its most precise form the pain extends across the precordium to the left shoulder and upper medial side of the arm and may extend as far as the elbow, the wrist or the fingers It may affect the wrist and fingers without involving any other portion of the extremity Sometimes the pain starts in the left wrist, arm or shoulder and travels toward the sternum It may commence in the sternal region and pass directly toward the left scapular region.

The more severe pain of angina pectoris may be described as constrictive, pressing, choking or expanding. There may be a sense of a vise around the thorax Often the pain resembles that of gaseous distention and the patient tries to belch *and takes baking soda in attempts to obtain relief The pain may or may not* compel the patient to stop activity and to rest

A common characteristic reaction of the patient to the pain is the fear of immediate impending disaster, termed angor animi

Duration of the attack of angina pectoris which occurs during physical activity is less than 5 minutes. The attacks which occur while the patient is at rest last longer, often from 5 to 15 minutes or up to a half hour. When severe pain lasts for more than a half hour, an acute coronary occlusion is usually present

The frequency of the attacks of angina pectoris varies, the intervals depending to some extent on avoidance of the factors which excite the attacks Attacks may come each day, without apparent cause, or after performance of the essential physiologic functions

Walking, especially against cold wind, or walking rapidly is the commonest form *of bodily exertion producing the pain of angina pectoris* Under favorable walking conditions on level ground, one of these patients may walk a mile or more without discomfort Some patients have pain when they walk for only a short way during the early morning hours, and then are able to perform rather heavy manual work the rest of the day

After a meal less effort is required to provoke an attack than when the stomach is empty Straining at stool is sometimes responsible for an attack. Any or all emotional upsets, such as heated arguments, the excitement of card playing, grief and anger, and a variety of petty annoyances may induce an attack Not infrequently cardiac pain occurs during sexual intercourse

Excessive insulin dosage may induce attacks of angina pectoris

EXAMINATION There are no abnormal physical signs in patients who have uncomplicated angina pectoris

The blood pressure in about half of those who have angina pectoris is within the normal range The rest have hypertension

Ordinarily electrocardiographic studies are made while the patient is free from pain; then the tracings are often entirely normal. There may be abnormalities, however, of the T and Q waves or of the QRS complexes

Tests of Coronary Reserve and Coronary Insufficiency. There is a range in which increases and decreases of the amount of the coronary blood flow to the myocardium occur without the production of pain This range represents the coronary reserve. In those who have an impaired range of adjustment of the coronary *circulation*, the coronary reserve is diminished. Attempts have been made to establish for diagnostic purposes tests or methods which measure the degree of

insufficiency of the coronary circulation These tests are (1) exercise in graduated amounts and (2) the anoxemia test. Usually these tests are not required, and in a patient who has definite coronary disease, performance of any test is undesirable (see Tests of Cardiac Function, page 704).

The patient who has angina pectoris may scarcely be inconvenienced, or his activity may be involuntarily so restricted that he is a chronic cardiac invalid. Most patients, for at least a few years after the initial episode, remain capable of earning their livelihood at their usual occupation as they become accustomed to the range of bodily activities which can be performed without having pain

DIAGNOSIS The essential diagnostic features of angina pectoris are (1) the paroxysmal occurrence of the pain, (2) its brief duration, (3) its characteristic location, radiation and quality and (4) its precipitation by effort and relief by rest or nitrites

The diagnosis of angina pectoris should be made with reservation in a woman unless there is evidence of an underlying disease capable of producing coronary insufficiency

In a series of cases Parker, Dry, Willius and Gage observed that the average age at onset of the anginal syndrome was slightly earlier for men than for women. While there was wide variation in age of the patients at the onset of symptoms, 88 per cent of the patients were from 40 to 69 years of age. The ratio of men to women was 4 3 1

The highest mortality rate occurs in the first year following the establishment of the diagnosis of coronary arterial disease with angina pectoris Thereafter the yearly mortality rate is less than it was in the preceding year. The survival rates of women having the anginal syndrome are greater than those of men

When corrected for deaths not due to angina pectoris, the five-year survival rate of patients 30 to 39 years of age with the anginal syndrome is definitely shorter than when the disease manifests itself later in life

Such associated conditions as cardiac hypertrophy, well-defined hypertension, previous cardiac infarction, congestive heart failure and significant electrocardiographic abnormalities are clearly related to a higher mortality rate and lower survival rates

Acute Coronary Occlusion and Myocardial Infarction. An acute thrombotic occlusion of a major coronary artery by the development of a thrombus or by an intimal hemorrhage with swelling of the arterial wall, or by an embolus, is termed coronary thrombosis

The injury or necrosis of a portion of heart muscle because of an interruption or curtailment of its blood supply is infarction of the myocardium or cardiac infarction.

Acute coronary occlusion and myocardial infarction are not always associated Coronary occlusion may occur without an ensuing infarction, and myocardial infarction may develop in the absence of an acute coronary occlusion The same symptoms are associated with myocardial infarction whether or not it is due to an acute coronary occlusion

There has been a progressive increase in the reported incidence of coronary occlusion This rising curve of reported mortality has not yet leveled off and it will not level off until clinical judgment in diagnosis supersedes diagnosis made by the electrocardiographic machine A person can die from some other cause despite the fact that he has a bad heart.

There is great uncertainty, however, as to whether this reported increase is real or is due to a statistical mirage produced by increased knowledge and more accurate diagnosis of coronary thrombosis The increase in the span of life due to the reduction in diseases of childhood and other infections and to other advances in medical knowledge has brought a larger proportion of the population to the age

groups in which death from arteriosclerotic coronary thrombosis occurs There h[illegible] always been a large number of individuals in the age group in which death fro[illegible] arteriosclerosis and coronary thrombosis is frequent, and probably there has bee[illegible] but little change in the mortality rates from arteriosclerosis or its complications [illegible] the total numbers in this age group.

Arteriosclerosis of the coronary arteries is usually responsible for acute coronar[illegible] occlusion The occlusion is caused by intimal hemorrhage and subsequent forma[illegible] tion of thrombus originating secondarily in an atherosclerotic plaque or in ruptur[illegible] of an arteriosclerotic abscess.

There is a basic relationship of hypertension and arteriosclerosis to acute coronary occlusion This relationship seems to be founded on observation that hypertension intensifies or accelerates arteriosclerosis. In some instances it seems that hypertension predisposes to the arteriosclerosis, and as a result of arteriosclerosis there are an intimal hemorrhage in arteriosclerotic plaques, formation of thrombus, and coronary occlusion There are other conditions which seem to predispose to arteriosclerosis, such as diabetes, familial hypercholesterolemia with xanthomatosis, myxedema, and polycythemia to mention but a few. Then there are those conditions which may seem to be important in the production of coronary occlusion and these may be separated into remote and immediate causes The *remote causes* may be enumerated (1) At least 9 of every 10 who have acute coronary thrombosis and myocardial infarction are between the ages of 40 years and 70 years When younger persons have acute coronary thrombosis, death often occurs suddenly (2) Most of those who have coronary thrombosis are men (3) Occupation is secondarily an important predisposing factor, for the reason that those who are temperamentally fitted for occupations requiring nervous tension are those who would have coronary thrombosis anyway (4) As statistical data accumulate, racial predilections become less obvious (5) Morbid heredity appears to be a remote etiologic factor predisposing to the occurrence of general arteriosclerosis, and therefore of coronary sclerosis and occlusion. (6) Patients who have acute coronary thrombosis often are of short, stocky stature, have some obesity, a thick short neck and a barrel-shaped thorax These somatic attributes are inherited The disease occurs, however, in all the somatic types.

Like the remote causes for coronary occlusion which have been enumerated some of the so-called immediate causes have only slight demonstrable relationship to coronary occlusion The actual occlusion of a coronary artery precedes the symptoms of the attack often by days Efforts by the physician to discover the immediate causes by recording the events or activities immediately preceding an acute coronary occlusion are futile The history will reveal (1) Physical exertion may be indirectly related to the development of a myocardial infarct after an acute coronary occlusion has already occurred (2) Emotional strains must be interpreted in terms of their effect on the individual and his reaction to them Like physical exertion, emotional stress cannot have a definite value assigned to it (3) Surgical operation may be followed by an acute myocardial infarction. Those affected usually are more than 50 years old and often past 60 years Almost always there is evidence in these hearts that there was pre-existing severe coronary arteriosclerosis, and often a previous coronary occlusion. (4) A patient who has had a certain attack of coronary occlusion confronts increased risk on subjection to surgical operation (5) There is no good evidence that the use, even the excessive use, of tobacco or overindulgence in alcoholic beverages contributes, either remotely or immediately, to the development of coronary artery diseases or acute coronary occlusion

PATHOLOGY A common cause of coronary thrombosis is the formation of a thrombus on an arteriosclerotic intimal plaque

Coronary occlusion occurs with equal frequency in the left anterior descending artery and the right circumflex artery. Occlusion of the left circumflex coronary artery

occurs less frequently Cardiac enlargement or hypertrophy occurs in at least two thirds of those who have had cardiac infarction However, the heart often remains of normal size after acute coronary occlusion. Cardiac hypertrophy is seen pathologically and cardiac enlargement is observed clinically in many cases of coronary occlusion

SYMPTOMS In most of those who have not had angina pectoris, premonitory thoracic pain precedes coronary occlusion by one to several days or weeks. Those who have had angina pectoris realize from the beginning that the pain of coronary occlusion is different from the pain of angina pectoris. It is distinctive because for

only to recur for hours or days at irregular intervals thereafter.

In some patients there is intense pain for one or two hours, after which the patient may feel and appear perfectly well Only electrocardiographic studies disclose that the pain was due to an acute myocardial infarction The pain of acute myocardial infarction, like that of angina pectoris, may extend to the shoulders and both upper extremities, to the neck and jaw, and to the interscapular region.

After myocardial infarction the patient who has not previously had pain may become subject to paroxysms of angina pectoris. These may occur as a result of *slight activity, meals or emotional states. Other patients previously affected by* attacks of angina pectoris may be completely relieved of their pain after they recover from the acute myocardial infarction

When myocardial infarction occurs without pain, it is often characterized by a sudden development of weakness, shock, pulmonary edema or congestive heart failure However, milder manifestation of myocardial infarction occurs during which the patient complains of transient cold sweats and weakness, and of feeling sick, dizzy, faint or nauseated Vomiting and thirst are common

When shock occurs, it comes soon after the onset of the pain and lasts from a few hours to one or two days or until death. If the patient recovers from the shock state, there is an awareness of pressure pain over the sternum or precordium, pain or weakness in the arms or forearms, or numbness in the wrist or fingers The persistence of shock is followed by congestive heart failure.

In some patients who have myocardial infarction the first manifestation is an abrupt attack of pulmonary edema which appears suddenly and without warning Sometimes, however, it follows hours or days after premonitory substernal pain or recovery from the earlier stage of shock

A myocardial infarction which commences with massive pulmonary edema may terminate rapidly or, if improvement supervenes, there may remain left ventricular failure characterized by recurrent cardiac asthma, orthopnea or dyspnea on slight exertion As time passes and subsequent infarctions occur, evidences of right-sided congestive heart failure ensue

EXAMINATION On examination there may not be present any abnormalities in appearance or behavior except that the patient complains of persistent thoracic pain Often there are evident weakness, perspiration, nausea, or abdominal distention and breathlessness

In other patients who have myocardial infarction the physician may witness all the known emotional and physical acrobatics which have been and are practiced by mankind when recipients of torture and pain The emotional response of terror dominates Generally, however, the patient is listless or prostrated. The responses to questions are brief. There is evident desire on the part of the patient to be left alone and not be burdened with answers to questions or examinations. The skin of the face is of ashen pallor and the lips and finger tips are faintly cyanotic. A bluish red mottling of the skin (cutis marmorata) is common. The hands and feet and the tip of the nose are cold and moist

In acute pulmonary edema the patient is propped up in bed, gasping for breath, and neck veins are engorged, the lips and skin distinctly cyanotic There is a cough and the sputum is frothy and pink with blood If death is impending, there is a copious foamy pink-stained fluid bubbling from the mouth and sometimes from the nose Pulmonary edema often clears rapidly after an opiate or bloodletting (500 ml) It may persist intermittently for several days despite any known therapeutic measures

On percussion of the cardiac borders and palpation of the apical impulse in cardiac infarction there may be no evidence of cardiac enlargement In the presence of congestive heart failure the heart may be so enlarged that this is readily determined by percussion and palpation.

Auscultation may reveal enfeebled heart sounds The first sound is usually faint and low pitched A soft blowing murmur at the apex is heard in instances of second or multiple infarction in which there is some degree of left ventricular dilatation and subsequent mitral insufficiency An aortic systolic murmur may be heard which is attributed to arteriosclerotic changes in the ascending aorta When hypertension persists despite the myocardial infarction, the second aortic sound is accentuated or reduplicated In left ventricular failure accompanied by pulmonary hypertension the second pulmonic sound is accentuated and may be louder than the second aortic sound

Gallop rhythm and pericardial rub if present are best heard at or slightly medial to the apex or in the fourth interspace near the left sternal border. The gallop rhythm is usually present when there is heart failure It most frequently appears in the first day or two after the infarction and disappears as cardiac function is improved and the pulse decreases

An intermittent pericardial rub is present in about one fifth of those who have cardiac infarction It may first be audible a few hours after the attack, but most commonly on the second or third day In large infarcts or progessive myocardial infarction a pericardial rub persists continuously for many days *It is usually heard* along the left border of the sternum, but it may be audible over a large part of the precordium The rub indicates an acute fibrinous pericarditis and not necessarily anterior infarction

The pulse rate often is between 100 and 110 per minute A sinus bradycardia with a pulse rate of 60 per minute may be present

In cardiac infarction there is first a rise in blood pressure. This is followed by a fall in blood pressure which occurs sometimes after several hours, but more often on the second day after the attack. The decrease in blood pressure is by progressive decline, and rarely it is delayed for a week. In those in whom it results early the blood pressures may be less than 90 or 80 mm of mercury In about one third of the patients who have had hypertension before myocardial infarction, the blood pressure remains within a normal range for at least many months thereafter In these there is no evidence of a diminished cardiac output. Some never regain their hypertension.

Acute cardiac infarction is accompanied by fever which begins within a few hours up to two days The temperature ranges from 100 to 102 F (37 7 to 38 8 C) or higher It usually reaches its peak on the third or fourth day and continues so for seven or eight days.

An increase in the *leukocyte count* occurs on the second or third day, only occasionally within hours after the infarction. The count varies from 12,000 to 15,000 or 20,000 per cubic *millimeter of blood. The leukocytosis disappears* by the end of a week. There is an associated polynucleosis with a slight shift to the left. A persistence of a high leukocyte count suggests the development of a complication such as pulmonary or other embolism, bronchial pneumonia, or progressive myocardial *infarction.*

The rate of sedimentation of the erythrocytes is almost always increased after an acute myocardial infarction This test is of questionable diagnostic value since the sedimentation rate may be increased in almost every illness which affects the human race and at times when no illness can be assigned.

Chemical examination of the blood may reveal hyperglycemia and azotemia which may prove to be transient unless present prior to the attack.

The examination of the urine usually reveals no significant abnormality indicative of cardiac infarction Hematuria may appear as a consequence of renal infarction, secondary to emboli arising from left ventricular mural thrombi

Electrocardiographic Changes in Acute Cardiac Infarction. The electrocardiographic changes following cardiac infarction, when studied early and by serial examination at brief intervals, may be specifically diagnostic of the disease. When coronary occlusion occurs without infarction, there may be no significant electrocardiographic abnormality despite the occlusion

Electrocardiograms are often normal with slight coronary heart disease, but in advanced disease they usually show changes in the Q and T waves and often in the S-T segments They may show the presence of intraventricular block and low voltage, uncommonly there is auriculoventricular block Abnormal left axis deviation is not common unless there is an associated hypertension

In the presence of coronary artery occlusion Q waves tend to appear or are exaggerated and the T waves may be deformed, becoming low, inverted, or of unusual shape A few hours after onset a high origin of the S-T segment from the descending limb of the R wave in lead I or lead III with a corresponding depression of this S-T segment in the opposite lead, that is, lead III or lead I appears With this change in the S-T segments and T waves there appears a distinct Q wave in the QRS complex, or an exaggeration of it if already present, in lead I when the S-T segment is elevated in lead I and in lead III when the S-T segment is elevated in that lead In the apex lead (lead IV) the R wave tends to disappear, the S-T segment is much elevated in the early stages and the T wave becomes inverted in the Q_1T_1 type of electrocardiogram, while the QRS and T waves remain unchanged or are exaggerated and the S-T segment occasionally is definitely depressed at first in the Q_3T_3 type After a few days the S-T segment begins to flatten out but there remains either in lead I or in lead III an inverted T wave The flattening or inversion of the T wave may persist, or the deflection may gradually become normal again after weeks or months, associated with recovery and repair of the infarct The abnormality of the Q waves often is permanent and remains as mute evidence of an old infarction

Infarction of the anterior wall of the left ventricle is generally attended by high origin and later inversion of T_1, development of Q_1, absence of R_4, and inverted T_4, while infarction of the posterior wall of the left ventricle is likely to be followed by high origin and later inversion of T_3 with development of a prominent Q_3 and a relatively normal lead IV The QRS and T waves in lead II may not be found altered, but it is common for T_2 to be flat or inverted during the course of the acute myocardial infarction and sometimes for months or years thereafter in either the anterior wall type of infarction of the posterior wall type, more commonly in the anterior wall type, the more marked and persistent the changes in lead I or lead III, the more abnormal is T_2

Electrocardiography of a suspected coronary heart disease is not complete without at least one chest lead and several authorities believe that it is essential to take even as many as 6 and more recently 12 chest lead records, especially in doubtful instances where there is need to explore to establish the lead point nearest to the area of damaged muscle Thus the routine cardiac apex lead (lead IV) may demonstrate or confirm by absence of the R waves or by elevation of the S-T segments or by inversion of the T waves the presence of an infarct of the anterior wall of the left ventricle without bothering with any other precordial lead, but a lateral wall or septal infarct may require leads further to the left or to the right, and a posterior wall infarct may be shown only, so it is said, by an esophageal lead

In some instances the electrocardiographic changes may not be significant of acute myocardial infarction and thus do not disclose its situation This is particularly

true when there have been multiple infarcts. Also the presence of a bundle-branch block, extensive pericarditis, the administration of digitalis, or a decidedly transverse or vertical heart, each or in combination, will obscure the electrocardiogram so that localization of the infarct is impossible.

DIAGNOSIS OF ACUTE CORONARY OCCLUSION AND MYOCARDIAL INFARCTION In a middle-aged or older man severe, oppressive pain over the precordium or over the lower part of the sternum or more extensively over the anterior part of the thorax, lasting at least a half hour, and not relieved by the administration of nitrites, indicates in most instances acute myocardial infarction.

Myocardial infarction is suspected in a middle-aged person when unexpectedly and without apparent cause there are severe prostration and collapse

When an aging person begins to experience attacks of nocturnal dyspnea or dyspnea on mild exertion, and when these symptoms suddenly become more severe, and there is perhaps enlargement of the liver, engorgement of the peripheral veins or peripheral edema, the possibility of a recent cardiac infarction is likely.

In many instances of acute cardiac infarction the thoracic pain may have been mild and transient and will have been forgotten But if there should be the history of a sudden and unexplained extreme fatigability, weakness, attacks of dizziness or syncope, indigestion, short episodes of dyspnea and pallor or cyanosis, palpitation and a cardiac arrhythmia, myocardial infarction is a likely diagnostic consideration.

There may be, however, certain electrocardiographic findings which in themselves justify the diagnosis. The electrocardiographic studies are invaluable in the diagnosis of cardiac infarctions without pain.

PROGNOSIS IN ACUTE CORONARY OCCLUSION AND MYOCARDIAL INFARCTION The duration of life when acute cardiac infarction occurs is unpredictable because from the instant the infarction occurs there is the constant threat of sudden unexpected death, then and during convalescence and even thereafter during the lifetime of those who survive for years The mortality rate is 40 to 50 per cent within 4 to 6 weeks after onset

It is probable that if the milder instances of the disease were identified, the mortality rate from first attacks of acute myocardial infarction would not exceed 1 in every 10 It seems that survival is the rule after the first occlusion or even after successive occlusions which have given no symptoms.

Myocardial Infarction and Sudden Death. Visceral embolism and peripheral embolism associated with myocardial infarctions are common complications and often the immediate cause of death These emboli, in the following order of frequency, affect the lungs, the brain, the kidneys, the spleen, the intestinal tract and the arteries The embolus often lodges at the bifurcation of a peripheral artery. The commonest site is the femoral artery at the origin of the profunda femoris, and the next commonest sites are the common iliac, axillary and brachial, and popliteal arteries and the aorta Peripheral embolism which does not cause immediate death is often characterized by acute and excruciating pain, blanching of the affected area of skin, loss of sensation, coldness of the extremity, loss of arterial pulsation and later loss of motion of the affected muscles. However, it is important to know that peripheral embolism may not be accompanied by pain. In the course of serious or critical illnesses and particularly when the patient has severe pain, embolism may occur without complaint and the patient be found dead by a member of the family or an attendant of the sick Among the causes of sudden death are massive pulmonary and cerebral embolisms

The weakened ventricular wall, the result of infarction, may permit the formation of ventricular aneurysm

Sudden death may be caused by the rupture of a cardiac aneurysm Sudden death from rupture of the heart in the absence of cardiac aneurysm is of relatively common occurrence in the first few weeks after acute myocardial infarction

Ventricular fibrillation is a common cause of death after infarction.

Silent Coronary Occlusion. Painless coronary occlusion may occur, under circumstances which are unpredictable, in patients who have not had prior known heart or circulatory disease. The cause, however, is usually an atherosclerosis of the coronary arteries. Although the attack does not cause pain, it seems that these patients have difficulty in swallowing, and are subject to choking, gagging and, some of them, dyspnea These manifestations may be considered as equivalents of pain

Hypertensive Arteriosclerotic Heart Disease. Hypertension, arteriosclerosis, atherosclerosis and hypertensive heart disease may be related to bodily build and constitution These may be more frequently present in the obese and occur with some predilection for the short, short-necked, stocky individual But are not short, stocky individuals predominant in the general population?

Hypertension, arteriosclerosis and atherosclerosis are uncommon before the age of 20 years Before the age of 20 years hypertension occurs chiefly with coarctation of the aorta, with acute or chronic glomerulonephritis, and rarely with endocrine tumors Thereafter it is encountered in 20 to 25 per cent of the general population and in 40 to 60 per cent of those more than the age of 50 years.

Atherosclerosis occurring before the age of 20 years is usually associated with diabetes mellitus or xanthomatosis of the congenital variety or a combination of diabetes and xanthomatosis. Atherosclerosis in the youth may or may not be asso- [illegible]

C[illegible] Disease. In hypertensive heart disease [illegible] doing its work (compensated), or it is [illegible] Unless increased or excessive demands are made on the heart in compensated hypertensive heart disease, symptoms may long be delayed When symptoms do make their appearance, they are those of left ventricular heart failure.

In the compensated stage of hypertensive heart disease the left ventricle is enlarged. Left ventricular hypertrophy is suggested by a forceful apical impulse, due partly to rotation of the apex nearer the thoracic wall and partly to a more forceful systolic contraction. The second aortic sound is accentuated Compensated hypertensive heart disease does not, in itself, cause murmurs, but an apical or basal systolic murmur may be caused by mitral or aortic sclerosis and calcification In elderly patients who have severe hypertension and pronounced dilatation of the ascending aorta, so-called arteriosclerotic aortic diastolic murmur is heard occasionally.

Elongation of the aorta as it loses its elasticity, attended by palpable pulsations in the episternal notch, with concomitant elevation of the subclavian, carotid and innominate arteries gives rise to strong arterial pulsations in the neck The carotid arteries are occasionally distorted and kinked in such a manner as to produce localized pulsating bulges which may resemble an aneurysm. A congenitally long carotid artery may cause a comparable pulsation

Increased pulsation of the aorta is common in hypertension In cases of longstanding hypertension and aortic arteriosclerosis, elongation and elevation of the aortic shadow are frequently observed roentgenoscopically.

In one fourth to one half of those who have moderate hypertension or arteriosclerosis or a combination of these conditions the electrocardiogram reveals no abnormality Often there is only a left axis [illegible]

[illegible] [illegible] [illegible]pensation in the hypertensive heart is almost always associated with advancing coronary arteriosclerosis Heart failure involves the left ventricle, but later there is evidence of congestion in the systemic circulation as well as in the pulmonary circulation

The hypertensive individual is characterized as a hyperreactor with exaggerated response to various influences, such as cold and epinephrine.

PATHOLOGY In hypertensive heart disease there is hypertrophy of the left ventricle When heart failure comes to those who have hypertension, there are present both dilatation and hypertrophy The left ventricle is primarily affected. The right chambers too may be dilated and hypertrophied as right heart failure is inevitable and when it develops it persists

Coronary arteriosclerosis with or without severe narrowing and with or without occlusion and infarction may be present, and may be the immediate cause of heart failure in hypertension Ischemic necrosis occurs in the hearts of those who have malignant hypertension

It is during the stage of acute heart failure that pronounced cardiac enlargement occurs A systolic murmur if present is often due to functional mitral insufficiency. Gallop (3 1) rhythms and pulsus alternans are common With pulmonary congestion the second pulmonic sound may be louder than the second aortic sound despite systemic arterial hypertension. Auricular fibrillation occurs in 1 of every 4 of those who have hypertensive heart disease Frequently it seems to precipitate heart failure.

The lungs contain water, and there is often edema of the dependent parts.

The combination of diastolic hypertension and left ventricular hypertrophy together with evidence of angina pectoris or coronary occlusion and myocardial infarction, and congestive heart failure or electrocardiographic signs of intraventricular conduction disturbances, or both, should permit of a diagnosis of hypertensive and arteriosclerotic heart disease if aortic stenosis is excluded.

Survival for 10 to 20 years and even 30 years is not unusual In the malignant phase of hypertension, characterized by diastolic pressure of 130 mm. of mercury or more, neuroretinitis and progressive renal insufficiency, the prognosis is grave

THE ENDOCARDIUM

Endocarditis. The term endocarditis is used with the appropriate adjective (bacterial, viral, spirochetal, rickettsial or mycotic) in connection with diseases of the endocardium due to a known causative organism. The term nonbacterial endocarditis designates an endocarditis usually associated with rheumatic fever or some general disease, perhaps the result of a bacterial sensitization reaction, such as rheumatic endocarditis and the endocarditis of Libman-Sacks Nonbacterial thrombotic endocarditis occurs in terminal or cachectic conditions Degenerative alterations of the endocardium are common These include endocardial sclerosis, calcification, ossification, fatty degeneration, and amyloidosis

The presence of superficial excrescences, verrucae, on the surface of the valvular or occasionally on the parietal endocardium, is the obvious feature of an endocarditis Valvular endocarditis may occur without the formation of verrucae, or verrucae may be present on one or more of the valves while other valves are free

Acute Bacterial Endocarditis. Bacterial endocarditis occurs in acute and subacute forms The acute forms of disease are mentioned in association with descriptions of the causative organisms. The disease occurs when there is bacterial invasion of the blood stream, with localization of the bacteria on the endocardium Once the bacteria are seated on the endocardium, there are persistent bacteremia, toxemia and embolization due to the bacterial vegetations breaking away from the endocardium Acute bacterial endocarditis is characterized by having been preceded by a local or a general infection Many of these patients have had previous endocardial disease Many of them, too, have normal hearts at the beginning of the acute endocarditis.

Acute bacterial endocarditis is commonly due to hemolytic streptococci, pneumococci or *Staphylococcus aureus*. The hemolytic streptococci belong serologically to Lancefield's group A, but occasional instances due to streptococci of group C or B subsequent

to abortion or delivery occur. Pneumococci responsible for acute bacterial endocarditis are usually aerobic but may be anaerobic.

Among a variety of other organisms responsible for acute bacterial endocarditis are *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Escherichia coli*, *Pseudomonas aeruginosa* (*Bacillus pyocyaneus*), *Klebsiella pneumoniae* (Friedlander's bacillus), *Actinomyces bovis*, *Micrococcus rugatus*, spirilla and *Bacillus anthracis* Many of this latter group may produce either an acute or a subacute bacterial endocarditis

Age, sex and race do not appear to be significant predisposing factors

In acute bacterial endocarditis the vegetations may be superimposed on thickened, scarred, vascularized, rheumatic valves or on congenital cardiac lesions or they may be on valves with little, minimal or no previous deformity. The pneumococcal and gonococcal infections often occur on previously normal valves and they affect the aortic valve more frequently than do the other organisms. Vegetations on the right side of the heart are caused most often by the gonococcus.

Ulceration is a feature of the acute form of the disease, valvular destruction being especially severe in the pneumococcal and gonococcal infections. The interventricular septum and rarely the cardiac wall may be perforated An accompanying pericarditis is a common finding.

The *spleen* is enlarged and may contain small abscesses. The *liver* may disclose focal or diffuse areas of necrosis and degeneration. The *kidneys* often present hemorrhages, infarcts and sometimes small or large abscesses One large abscess, renal carbuncle, may occur in staphylococcal septicemia Multiple renal abscesses are characteristic of this septicemia There may be a focal or acute diffuse glomerulonephritis The *eye* may be affected by panophthalmitis, but more commonly there is simply a choroiditis

The general symptoms are those of the primary infection which has originated the bacteremia During the course of such an infection a chill and fever may signify the beginning of the septicemia The fever then persists despite the disappearance of the original focus of infection which seems to have healed In other instances, during the course of an infection, there are chills, profuse sweats, marked weakness and various cerebral and psychic disturbances, embolic and vascular symptoms consisting of vascular occlusions in parenchymatous organs, or in the extremities, and cutaneous lesions The vascular occlusions may affect the brain, producing hemiplegia There may be occlusion of peripheral arteries Pulmonary infarctions causing hemoptysis are common All of these complications give their respective localizing symptoms

On examination cutaneous manifestations consisting of petechiae, hemorrhages, and erythematous, bullous and purulent lesions may be evident The spleen may be palpable The other physical findings are those of the original focus of infection This focus may not be evident

The heart rarely contains any physical abnormalities which are of significance There may be a systolic murmur or an increase in intensity of one which may have been present. There are a rapidly developing anemia, a leukocytosis and perhaps a positive blood culture

In acute bacterial endocarditis the culture of organisms from the blood stream confirms only the diagnosis of a bacteremia. The appearance of successive generations of white-centered cutaneous petechiae in a patient who has a proved bacteremia is very suggestive that the endocardium is likewise affected If on ophthalmoscopic examination petechiae are present in the choroid or if a panophthalmos develops, acute bacterial endocarditis is a likely diagnosis

Subacute Bacterial Endocarditis. In 9 of every 10 who have subacute bacterial endocarditis the causative organism is a nonhemolytic streptococcus. The causative organisms in the rest of those who have subacute bacterial endocarditis comprise a great variety of microorganisms. Almost any organism capable of producing septicemia may cause subacute bacterial endocarditis

Subacute bacterial endocarditis almost always affects a heart which has valvular defects, usually acquired from an earlier rheumatic fever A few patients in the

younger age groups have congenital cardiovascular anomalies which predispose to subacute bacterial endocarditis

Subacute bacterial endocarditis often develops after some inconsequential event such as the extraction of a tooth or the removal of tonsils, or a bad cold, especially in those who have rheumatic or congenital cardiac valvular defects.

The highest incidence of this disease is from 20 through 29 years of age, but subacute bacterial endocarditis may occur at any age from early childhood to late in life. There is a somewhat higher incidence among men than among women

PATHOLOGY. The vegetations are usually situated on the leaflets of the mitral valve but may affect any or all of the valves.

The myocardial lesions consist of small infarctions, bacterial embolization of arterioles and capillaries, necrosis of the walls of these small vessels, and surrounding inflammatory reactions

In subacute bacterial endocarditis often the *kidneys* may present diffuse petechial hemorrhages which produce depressed, yellowish, sharply demarcated lesions of the cortex indicating the sites of infarction The *spleen* is almost invariably enlarged and contains infarcts

Lesions of the *brain* are frequent and widespread. There is often a diffuse meningoencephalitis due to disseminated bacterial embolization of arterioles and capillaries Embolic lesions of the large cerebral arteries are common and in some cases prove fatal Bacterial emboli lead to mycotic aneurysms and thrombosis Cerebral, intraventricular or subarachnoid hemorrhage may result from rupture of a mycotic aneurysm Encephalomalacia is a consequence of vascular (embolic) occlusion Occasionally small or large cerebral abscesses are formed

In the lungs congestion, pulmonary emboli and infarctions, and bronchopneumonia may be present The liver is enlarged and engorged owing to chronic passive congestion The stomach and the intestines almost always are involved during the course of subacute bacterial endocarditis, the involvement originates from embolic phenomena Bacterial emboli also affect the large or small arteries of the extremities causing circulatory disturbances and, in some, gangrene

SYMPTOMS The symptoms of subacute bacterial endocarditis are referable to the general infection, to the embolic and vascular phenomena and to the affected heart The onset is usually insidious It may commence acutely, however, with chills and high fever An acute onset is generally due to embolus in a cerebral, an abdominal or a peripheral vessel

At the onset fever is the most constant of all symptoms It may be continuous, remittent, intermittent or septic The temperature is rarely more than 103 F (39 4 C), the usual range is between 100 and 102 F (37 7 and 38 8 C) Periods of apyrexia lasting for weeks at a time often supervene Shaking chills or chilly sensations are common During the chill the temperature is likely to reach 104 to 105 F (40 to 40 5 C) with quick rise and sudden fall of the temperature Profuse night sweats, even in the absence of known fever, are common Pallor, weakness, headaches, tenderness over the long bones and the sternum, breathlessness and easy fatigability are common subjects for complaint

Anorexia, abdominal pain, nausea and vomiting are common and diarrhea may be severe For weeks in the beginning of the disease, diarrhea and fever may be the only symptoms

Splenic infarction may be characterized by sharp sudden pain in the left side of the hypochondrium or the lower part of the left axilla which may extend to the left shoulder or precordium. There may be local soreness and hypersensitivity of the skin over the splenic region

Cerebral or spinal cord infarction may be manifest by the sudden occurrence of hemiplegia or monoplegia In the symptomatology of subacute bacterial endocarditis it is well to be aware that many of the emboli reach small arteries and cause localized symptoms more frequently than they reach the arteries to vital organs and produce alarming symptoms.

Examination. The *skin* is pale and often there are petechiae. The petechiae are most frequently and best observed in the conjunctiva, especially of the lower lid, in the oral mucosa and on the soft and hard palates, in the fundus, in the skin about the clavicles and in the lower extremities Some petechiae may have white centers Petechiae occur in successive generations. Each generation disappears after several days, to be succeeded by another at some future date.

Tender cutaneous lesions which are raised, swollen patches from a few millimeters to 0.5 cm in diameter, bluish, or pink or red, occur in the pads of the fingers or toes, in the thenar or hypothenar eminences, on the soles of the feet, or between the toes These lesions are always tender. It seems that these tender nodes when present are pathognomonic of subacute bacterial endocarditis.

The cardiac findings are those of the existing valvular disease or congenital malformation. In the beginning of subacute bacterial endocarditis valvular lesions may be present of which the patient is unaware As the heart is repeatedly examined during the progress of the disease, there are changes in the character and sites of murmurs, or new murmurs develop. A new murmur, rough in tone, which appears suddenly may be due to rupture of a chorda tendinea or perforation of a valve cusp.

Jaundice may be present and the liver may or may not be palpable The jaundice may be associated with pulmonary infarction or with gonorrheal endocarditis. The spleen is palpable in at least two thirds of those who have subacute bacterial endocarditis

Clubbing of the fingers and of the toes is frequent

Sudden blindness and ophthalmitis may result from embolism of the central retinal artery Visual field defects and fever when of sudden onset may be suspected as being the result of subacute bacterial endocarditis Retinal hemorrhages may be present (see Diseases of the Eye, Chapter 4)

Anemia is a common feature of the disease Leukocytosis is not characteristically present unless there is some complication The sedimentation rate of erythrocytes seems to be accelerated in subacute bacterial endocarditis Polymorphonuclear leukocytosis is slight if present at all Blood cultures are found to be positive in 9 of 10 who have the disease. Cultures may have to be repeated before positive ones are obtained

The urine may contain blood and albumin especially after infarctions of the kidneys There may be a focal glomerulonephritis present

Diagnosis The diagnosis of subacute bacterial endocarditis is based on the presence of (1) a positive blood culture, (2) embolic phenomena, (3) a febrile course and (4) a valvular defect or congenital cardiovascular lesion The diagnosis of subacute bacterial endocarditis should be assumed as most probable whenever a patient who has an organic cardiac murmur experiences fever, without apparent cause, for more than one week

Blood cultures have acquired additional importance above that of diagnosis because beneficial treatment is most likely when the causative organism is identified and its sensitivity to individual antibiotics is determined

VALVULAR HEART DISEASE

There are two types of valves in the heart the bicuspid (mitral) and the tricuspid between the atria (auricles) and the ventricles, and the two sets of semilunar valves at the entrance of the pulmonary artery and aorta

The *bicuspid* or *mitral valve* is the most important and the most deeply seated It is situated under the edge of the left border of the sternum opposite the fourth costal cartilage It separates the left atrium and ventricle and lies nearly transversely

The *tricuspid valve* is situated under the middle of the sternum opposite the fourth intercostal space It runs obliquely downward and to the right from the third left intercostal space to the fifth right costal cartilage. It separates the right atrium and ventricle

The *pulmonary semilunar valve* lies opposite the sternal end of the third left costal cartilage. It is the most superficial valve and the one highest up on the sternum It prevents regurgitation of the blood into the right ventricle from the lungs

The *aortic semilunar valve* is situated under the left side of the sternum about level with the lower edge of the third costal cartilage.

Mitral Valvular Disease. Rheumatic endocarditis of rheumatic fever is responsible for almost all mitral valvular disease Mitral valvular disease occurs as (1) mitral insufficiency and (2) mitral stenosis

Mitral Insufficiency. This form of disease occurs as the result of imperfect closure of the valves The disease is called also organic mitral insufficiency and relative mitral insufficiency

In rheumatic fever there is first an organic mitral insufficiency Other causes for organic mitral insufficiency are bacterial endocarditis, traumatic rupture of a cusp or of the chordae tendineae, spontaneous rupture of the chordae, and rupture of a papillary muscle

Organic mitral insufficiency is consequent to incomplete closure of the mitral orifice which results from imperfect coaptation of the valve cusps because of scarring, thickening, shortening and deformity In others there are fusion and shortening of the chordae which fix the cusps and restrain their apposition so as to prevent closure of the valvular orifice In still others there exist inflammation and scarring of the mitral ring which dilate the orifice and interfere with the muscular systolic shrinkage in the size of the ring.

Rupture of the mitral valve may cause mitral insufficiency by perforation or tear of a cusp or by rupture of chordae or a papillary muscle Spontaneous rupture of chordae tendineae, usually of previously diseased valves, may occur.

Relative or functional mitral insufficiency occurs commonly as a result of great dilatation of the left ventricle in association with left ventricular failure. Imperfect valvular closure under such circumstances is due to dilatation of the mitral ring and to retraction of the cusps by the chordae and papillary muscles Relative or organic mitral insufficiency may be caused by any of the etiologic causes of heart failure; these are mainly rheumatic fever and arteriosclerosis.

The left atrium dilates and hypertrophies in both mitral insufficiency and mitral stenosis It may attain a volume of 2 or 3 liters In contrast, an advanced mitral stenosis may be present without atrial enlargement if the heart is generally enlarged

In hearts with predominant mitral stenosis the left ventricle is of normal size, or may be smaller than normal, or atrophic

Symptoms Many patients who have mitral insufficiency enjoy a normal life Compensation of mitral insufficiency is effected by dilatation and hypertrophy of both the left atrium and the left ventricle When symptoms appear, they are those of congestive heart failure

Examination On physical examination there may be only a loud, harsh or blowing systolic murmur near the apex, with varying degrees of transmission toward the axilla. A murmur which is not transmitted to the axilla is usually indistinguishable from insignificant functional murmurs

If roentgenoscopic examination reveals an enlargement of the left atrium and the left ventricle, the significance of the murmur is thus assured

If there is a rupture of the mitral chordae tendineae, the systolic murmur is loud and is associated with a thrill There may also be an associated apical diastolic murmur

Heart failure resulting from mitral insufficiency is rare. If heart failure should be present, it results from an active rheumatic myocarditis or an unusual strain such as may attend gestation.

The electrocardiogram in mitral insufficiency shows a tendency to left axis deviation. The P waves may be tall and notched.

DIAGNOSIS. The diagnosis of mitral insufficiency is based on the presence of an apical systolic murmur and enlargement of the left atrium and ventricle, and usually a history of rheumatic fever or chorea.

The diagnosis of mitral insufficiency due to nonrheumatic causes is based on the sudden development of a loud apical systolic murmur and thrill in the course of bacterial endocarditis or myocardial infarction, after thoracic injury, or after severe exertion

The presence of an apical systolic murmur in a patient who has hypertension or coronary artery disease and heart failure which disappears with improvement of the circulatory status, confirms the functional nature of the disturbance.

Calcification of the mitral cusps almost always occurs in organic rheumatic mitral insufficiency or stenosis.

If there is no more evidence of heart disease than a murmur, there is no certain method of differentiating whether the murmur is organic or functional in origin Functional murmurs are more commonly present than organic murmurs and are the loudest in the pulmonic region, transmit poorly and are faint in intensity. Cardiorespiratory murmurs disappear when the breath is held

Mitral Stenosis. Mitral stenosis is due mainly to rheumatic endocarditis but occasionally it is a congenital defect due either to anomalous development or to fetal endocarditis Rheumatic mitral valvular disease occurs much more frequently among girls and women than among boys and men

In mitral stenosis the mitral orifice is obstructed and too little blood flows from the left atrium into the left ventricle during ventricular diastole and, consequently, into the aorta in ventricular systole Hypertrophy and dilatation of the left atrium develop, and increased pressure in the pulmonary circulation and hypertrophy of the right ventricle ensue The right ventricle dilates when it becomes inadequate for the work required of it

Thrombi arising in the auricles occur at any stage of mitral stenosis, but they are especially frequent after right heart failure and development of atrial fibrillation. In the absence of right heart failure and consequent dilatation of the right atrium, the thrombi are usually confined to the left atrium

Embolization of the kidneys, spleen, hepatic artery, mesenteric artery and peripheral arteries occurs Embolization of the aorta with formation of a thrombus at its bifurcation may cause sudden sharp pain in the abdomen, lower part of the back, and the extremities, loss of pulsation and warmth of the lower extremities, and shock More localized symptoms occur with embolization of the popliteal, femoral or brachial arteries. Gangrene may result Subsequent emboli in other parts of the body may eventually cause death Extensive infarction of the lungs and spleen may occur in which minimal or no recognizable symptoms are present

A sudden hemiplegia may occur in the presence of a well-compensated mitral stenosis Sometimes these hemiplegias are relatively benign in that they clear up with but slight disability, only to be repeated. Occlusion of a small cerebral artery may occur, followed by only a focal paralysis or isolated aphasia

SYMPTOMS Often patients who have mitral stenosis have no cardiac symptoms and do not have a known history of rheumatic fever or chorea There is no manifest evidence of a decrease in the cardiac reserve. A normal life is, and has been, pursued Some of these men and women will be aged, but there is only a minimal degree of arteriosclerosis, such a slight degree that there is not the least suspicion that the cardiac signs are originating from this source.

Some of these patients, however, are not so fortunate, for there comes a time when cardiac compensation is imperfect The lungs become congested and attempts at unusual degrees of bodily exertion result in dyspnea

Mild degrees of disturbance of gaseous exchange in the lungs, for instance, at the stage of left atrial failure, may cause dyspnea and cyanosis A mild degree of cyanosis produces the so-called mitral facies, which is characterized by a cyanotic flush of the skin over the malar prominences and a dusky cyanosis of the lips which is most

evident after exertion Severe degrees of cyanosis are present in long-standing instances of mitral stenosis

Dyspnea on exertion is the commonest complaint of the patient who has mitral stenosis Many patients who have mitral stenosis become so accustomed to a mild degree of chronic dyspnea that they are scarcely aware of its presence.

Palpitation and precordial distress are early and constant symptoms The palpitation is especially disturbing at night; the patient often attributes it to indigestion The onset of auricular fibrillation may be described by the patient as palpitation Fibrillation, however, is usually established and associated with a slow ventricular rate for a long time without the patient's being aware of its presence

A cough worse at night and after physical exertion than at other times may be an annoying symptom Secondary bronchial and pulmonary infections are prone to complicate pulmonary congestion in mitral stenosis and these may be partially responsible for the cough

Hemoptysis may be the initial and only complaint. It may occur suddenly and be of considerable severity Hemoptysis has been attributed to the rupture of small congested vessels in the lungs, to the rupture of varices of the bronchial veins, and to pulmonary embolization and infarction The ultimate prognosis in those who have hemoptysis is poor

Acute pulmonary edema is much less frequent in mitral stenosis than in hypertensive heart disease or in aortic valvular lesions Pulmonary edema follows sudden or severe exertion, surgical operations, pregnancy, childbirth, attacks of paroxysmal tachycardia, or intravenous administration of physiologic saline solution

Angina pectoris when present is due to an associated aortic or coronary artery disease rather than to the mitral stenosis It is rarely present

Paralysis of the left recurrent (laryngeal) nerve may occur as the result of an enlarged left atrium pressing on the nerve The hoarseness may be intermittent at first but may progress to complete aphonia.

Examination In compensated mitral stenosis the pulse is generally normal Fibrillation, extrasystoles and dropped beats are frequent.

Auricular fibrillation is present in about half of those who have mitral stenosis The fibrillation may be paroxysmal at first but becomes persistent It may be an accompaniment of right heart failure or may actually precipitate it However, auricular fibrillation with slow ventricular rate is often compatible with years of comfortable life

The blood pressure in mitral stenosis is usually within normal limits However, a hypertension may be present in some instances.

In children the precordium may bulge Often there are visible pulsations, aside from those of the precordium, in the epigastrium and to the right of the sternum

A late diastolic (presystolic) thrill may be palpated as a vibrating sensation on the surface of the precordium in the region of the apical impulse A palpable shock may accompany the first sound at the apex and the second sound in the pulmonic region The apical impulse is usually felt at its normal site. After experience has been gained, a presumptive diagnosis of mitral stenosis can sometimes be made from palpation alone

The total area of cardiac dullness to percussion is often increased The increase in the area of cardiac dullness is along the left sternal border, at the level of the third interspace and fourth rib. This increase in dullness at the base of the heart is present in both mitral stenosis and insufficiency.

The first sound at the apex is short, loud and booming. A similar booming first sound may be heard in hyperthyroidism

The second sound heard over the pulmonic area is accentuated and may be accompanied by a palpable shock. The pulmonic second sound may be duplicated as well as accentuated.

There is a localized apical diastolic murmur. This may be late in diastole (presystolic), or it may fill most or all of diastole. It may occur in the early or middle period of diastole. The diastolic murmur presumably arises from the noise made by rapid blood flow past the mitral obstruction into the left ventricle. The time in diastole at which this murmur occurs is that at which the pressure difference between the left atrium and the left ventricle is excessive. This pressure difference is accentuated when the left atrium undergoes compensatory dilation and hypertrophy.

The late diastolic (presystolic) murmur in mitral stenosis is of a low tone with a crescendo accentuation merging into an abnormally loud first sound. The murmur is well circumscribed at or near the apex beat This diastolic (presystolic) murmur may be accentuated by a left lateral position, after exercise has quickened the heart rate This murmur is absent until the obstruction of mitral stenosis is significant, and it disappears at the onset of auricular fibrillation and heart failure.

A diastolic murmur (presystolic in time) may be heard in aortic insufficiency, severe anemia, acute nephritis with hypertension, and left heart failure as well as in mitral stenosis

An apical systolic murmur is frequently present owing to significant mitral regurgitation

On occasion a soft-blowing diastolic murmur, known as the Graham Steell murmur, is heard over the pulmonic region. It is probably the result of a functional insufficiency of the pulmonic valve due to pulmonary artery hypertension and consequent dilatation of that vessel and of the pulmonic orifice. The Graham Steell murmur is distinguished from the diastolic murmur of aortic insufficiency by differences in the roentgenologic appearance of the heart and by distinctive peripheral signs.

The roentgenologic appearance of the heart in mitral stenosis varies with the stage or severity of the lesion.

Calcification occurring on the mitral valves or on the annulus fibrosus in the aged is clinically unimportant Calcification of the mitral ring or cusps may be associated with aortic stenosis, also the result of calcification Deposits of calcium may be present in the fibrous septum which in time affects the bundle of His and thus heart block or other disturbances of conduction ensue

In the *electrocardiogram* in mitral stenosis the P waves in leads I and II are often widened and notched, and may be of increased voltage There is usually right axis deviation with evidence of right ventricular strain Occasionally there is evidence of right bundle-branch block. Auricular fibrillation is frequent.

Diagnosis The diagnosis of mitral stenosis is based on a history of rheumatic fever, on the foregoing described physical signs, and on roentgenologic evidence of a large left atrium. The diagnosis is more certain if the characteristic diastolic (presystolic) murmur is heard A sharp, snappy first sound at the apex following the second sound at the apex and a diastolic thrill further support the diagnostic evidence Electrocardiographic records showing right axis deviation, large, notched P waves and auricular fibrillation also suggest mitral stenosis, especially if there is a history of rheumatic fever

Aortic Valvular Disease. *Aortic Insufficiency.* Insufficiency of the aortic valve results from rheumatic fever, syphilis, bacterial endocarditis, trauma, severe hypertension and aortic arteriosclerosis, and dissecting aneurysm of the aorta Aortic insufficiency in patients less than 35 years old is almost exclusively rheumatic in origin and is combined with mitral valvular disease.

Some blood regurgitates from the aorta into the left ventricle during diastole. Since, in diastole, the ventricle also receives its normal amount from the left atrium, its cavity dilates At each systole a large amount of blood is delivered into the aorta, and the wall of the left ventricle hypertrophies.

The heart in aortic insufficiency is very large (oxheart or cor bovinum), weighing

from 500 gm. to 1,000 gm The enlargement involves the left ventricle and interventricular septum

SYMPTOMS If the left ventricle is normal and the mitral valve sufficient, a normal span of life may be expected without symptoms. In those who have compensated aortic insufficiency, the symptoms are often subjective and referable to the forceful ventricular contractions For instance, when the patient lies on the left side, the audible beat of the heart and cervical vessels is disturbing. The conventional crossed legs may be uncomfortable from the pulsating popliteal artery. Vascular pulsation of the uvula may cause an uncomfortable tickling in the throat.

Those who have rheumatic aortic insufficiency may have nocturnal angina pectoris accompanied by a rise in blood pressure, increased pulse and respiratory rate, palpitations, sweating, and flushing of the face In aortic insufficiency of syphilitic origin angina pectoris is often due to the frequency associated stenosis of the coronary ostia or to conventional atheromatous coronary heart disease.

A rapidly developing breathlessness on exertion is the first symptom of left heart failure in aortic insufficiency. The dyspnea may be paroxysmal, appearing suddenly while the patient is at rest as well as during activity. Paroxysmal dyspnea of short duration is characteristic of syphilitic aortic disease Orthopnea is soon added

EXAMINATION The pulse rate is normal in compensated aortic insufficiency. The pulse wave in aortic insufficiency rises and falls rapidly (Corrigan pulse). To find the so-called water-hammer pulse, it is well that the patient's arm be elevated above the head and the pulse palpated in this position

In aortic insufficiency there are marked pulsations in the vessels of the neck, in the temporal arteries and in other large vessels which may impart a to-and-fro motion to the entire head or to the leg when crossed over the opposite knee. Ophthalmoscopic examination reveals pulsations of the retinal arteries as well as of the veins

The capillary pulse may be observed in a normal person when the skin is warm In sickness the phenomenon is observed in fever, anemia, hyperthyroidism, and aortic insufficiency Capillary pulsation may be elicited in several ways: (1) by observing the nail bed or skin at the root of the nail while pressure is made on the tip of the nail, (2) by observing the edge of the blanched region when the mucous membrane of the lip is compressed by a glass slide, (3) by observing the earlobe or finger tip while it is being transilluminated by a weak source of light

The apical impulse is forceful and is situated to the left of and below its normal site It may be seen or felt in the left axilla. A diffuse systolic depression of the anterior thoracic wall, medial to the forceful apical beat, is caused by the wide excursions of the contracting ventricle within the closed thoracic cage

Percussion reveals an enlargement of the heart to the left and downward There is a soft, high-pitched diastolic murmur In syphilitic aortic insufficiency it is often louder and lower-pitched than in the rheumatic form of the disease. In traumatic aortic insufficiency the murmur is often extremely loud and has a pleasant quality It starts immediately after the second sound It is best heard in the second right intercostal space or along the left border of the sternum in the third or fourth interspace

A low diastolic blood pressure is regularly present in aortic insufficiency (60 mm. of mercury or lower) The systolic pressure is normal or increased and thus the pulse pressure is increased.

The diastolic murmur of aortic insufficiency is often a difficult heart murmur to hear. In searching for the murmur, ask the patient to stand, to bend slightly forward or assume the crawling position, and hold the breath intermittently during auscultation. A systolic murmur situated at the base of the heart when present may be helpful for purposes of timing the murmurs.

A late diastolic apical murmur (Austin Flint murmur) occasionally is heard in aortic insufficiency when there is left ventricular failure. This murmur is identical with the late diastolic (presystolic) murmur of mitral stenosis The mitral valve is normal, however, in those who have an Austin Flint murmur.

On auscultation over the femoral artery a booming sound synchronous with each pulse through the vessel may be heard. This sound has been described as resembling a pistol shot. In some instances a double sound (Traube's double tone) is heard in aortic insufficiency instead of the single pistol-shot sound.

A systolic murmur is present over the femoral artery in normal persons if the vessel is slightly compressed by the bell of the stethoscope In aortic insufficiency a diastolic as well as a systolic murmur is audible over the compressed vessel because there is a rapid diastolic regurgitation toward the heart as well as systolic forward passage toward the periphery This double murmur (Duroziez's sign) is not limited to aortic insufficiency but may also be present in hyperthyroidism, febrile states and anemia.

Diagnosis A diagnosis of aortic insufficiency can be made when there are enlargement of the left ventricle, a high-pitched but often scarcely audible diastolic murmur over the aortic region or along the left border of the sternum, and when present, peripheral circulatory phenomena There is an increased pulse pressure obtained by use of the sphygmomanometer.

Cardiac failure is an integral part of the course of aortic insufficiency, and there may be no significant symptoms before failure occurs Sudden death is frequent in this form of valvular heart disease

Aortic Stenosis. Rheumatic fever is the chief cause of aortic stenosis before the age of 50 years Aortic stenosis after the age of 50 years results from atherosclerosis

The heart in all forms of aortic stenosis is hypertrophied In the smaller hearts the hypertrophy is confined to the left ventricle In the larger hearts dilatation and hypertrophy involve the right ventricle as well as the left ventricle, and often the atria.

Complete heart block, bundle-branch block, intraventricular conduction defects and delayed auriculoventricular conduction frequently are present and result from an extension of the calcific process from the aortic valve to the fibrous septum

Symptoms Compensated aortic stenosis is asymptomatic When valvular obstruction develops then symptoms commence.

Cardiac pain is present in 1 or 2 of every 10 who have aortic stenosis Angina pectoris is more frequently suffered by those who have aortic stenosis than by those who have other valvular heart lesions

Dizziness, faintness and syncope associated with exertion or change of position may be the subject of complaint Convulsive disorders may occur as a part of the symptom complex of aortic insufficiency

Dyspnea on exertion is the first symptom of left heart failure in aortic stenosis. It may be present for months or even a year or two before the other symptoms commence In time nocturnal paroxysmal dyspnea (cardiac asthma) supervenes. Insomnia, nightmares, cough and expectoration, occasional hemoptysis, and orthopnea are symptoms of heart failure and are common in aortic stenosis

Examination The pulse in advanced aortic stenosis is of small amplitude, rises slowly and falls away slowly (pulsus parvus et tardus) Its slow maintained elevation imparts to it the form of a plateau. There is a delay in arrival of this slow small pulse at the wrist.

The blood pressure in aortic stenosis may be within normal limits The systolic pressure may be slightly diminished, and the diastolic slightly elevated, with a resultant small pulse pressure, even though these pressures are still within the range of the normal limits The systolic pressure on the average is increased

Palpation often reveals a systolic thrill at the base of the heart, to the right of

the sternum or along the right cervical vessels. This thrill is best felt if the patient sits or stands and bends forward.

Over the aortic region there is a loud, long systolic murmur which is rough in quality and is transmitted to the neck and to the left axilla The murmur may be heard downward along the sternum toward the apex and occasionally in the left infrascapular region in the back. A diastolic murmur over the base of the heart often is present

The second sound over the aortic area is normal or is heard with difficulty or it is absent.

The presence of effusions in the serous cavities, particularly hydrothorax, cyanosis, weakness, loss of weight and emaciation, portend an impending disaster. Sudden death is common in this disease

Roentgenologic examination reveals that in size the heart is either normal or diminished

The electrocardiogram may reveal normal conditions or may show only a left axis deviation if there is no associated mitral stenosis However, there may be permanent or transient conduction disturbances and abnormalities of the T waves and RS-T transitions

DIAGNOSIS In aortic stenosis a loud, rough, aortic systolic murmur, an aortic systolic thrill, absent or faint second aortic sound and a small, delayed pulse suffice to justify the diagnosis The finding of calcification of the aortic valves on roentgenologic examination is confirmatory In the presence of mitral stenosis the diagnosis is often impossible to make.

Those who have a calcific form of the disease have a good prognosis The outlook remains favorable so long as compensation is maintained Heart failure is usually fatal in this disease

Tricuspid Valvular Disease. Organic tricuspid insufficiency is generally caused by rheumatic fever In some instances it may result from trauma or congenital malformation. Occasionally a functional tricuspid stenosis originates from bacterial vegetations or thrombi Still more rarely tumors projecting into the tricuspid orifice cause an insufficiency The tumors may be primary myxoma or sarcoma or secondary metastatic lesions of hypernephroma, sarcoma of the testis, carcinoma of the thyroid or other neoplasms

The usual age of incidence is between 25 years and 40 years, but occasionally the disease is present in persons more than 50 years of age Women are more commonly affected than men

Tricuspid insufficiency and stenosis are usually a part of rheumatic fever The right ventricle may be normal in size or only slightly hypertrophied but usually it is both dilated and hypertrophied The venae cavae are dilated Systemic venous distention occurs early The liver, spleen and kidneys reveal chronic passive congestion Cardiac cirrhosis of the liver is frequent

The dynamics of tricuspid lesions may be modified and are often dominated by those of an associated mitral or aortic valvular disease.

SYMPTOMS The symptoms of tricuspid valvular disease are those of right-sided heart failure with systemic venous engorgement.

EXAMINATION On examination there is cyanosis which is more pronounced in those who have tricuspid and mitral stenosis combined than in patients who have mitral stenosis alone Jaundice may be present

In tricuspid insufficiency the negative venous wave is replaced by the so-called positive venous pulse This positive venous pulse is often visible as a broad systolic wave ascending the neck along the course of the internal jugular vein up to the ear

In tricuspid insufficiency there is usually a palpable pulsation of the liver during ventricular systole. The systolic hepatic pulse is elicited as an expansile sensation when one palm is held over the posterolateral surface and the other anteriorly over

the liver. Practice is required to attain sufficient skill to elicit this pulse. Hepatic enlargement is constant. There often is ascites.

In primary tricuspid stenosis and in tricuspid insufficiency peripheral edema may be absent. In cases of functional tricuspid insufficiency edema may be absent but it is usually present

Percussion reveals an enlarged heart The right border may reach the right midclavicular line indicating a constant and definite cardiac enlargement.

The findings revealed by examination in tricuspid valvular disease are often determined by the associated mitral stenosis or other valvular disease When tricuspid insufficiency is manifest, there may be a reverberatory movement of the thoracic wall due to a pulsating liver, and ventricular systoles.

The tricuspid lesion may produce a systolic murmur over the lower end of the sternum or adjacent to it. This murmur is indistinguishable from a mitral murmur. When tricuspid stenosis is present a diastolic murmur may be heard which may be accompanied by a thrill However, these findings are usually those of mitral stenosis or of mitral and aortic disease.

The electrocardiogram reveals a right axis deviation and inversion of the T wave in lead III and often also of the T wave in lead II. There may be wide, notched and high voltage P waves when there is sinus rhythm. Auricular fibrillation is common

Diagnosis. The presence of systemic venous congestion, cyanosis, ascites and valvular heart disease is sufficient for a presumptive diagnosis of tricuspid heart disease The roentgenogram reveals clear lungs and enlargement of the right atrium.

Functional tricuspid insufficiency often signifies the end stage of chronic valvular heart disease or pulmonary disease and therefore is always serious.

Differentiation of tricuspid valvular heart disease from constrictive pericarditis is difficult In constrictive pericarditis the heart is not enlarged and evidence of organic cardiovalvular disease is absent

Organic tricuspid valvular disease may be compatible with life for a long period during which the only discomforts, if any, result from venous engorgement punctuated by recurring ascites.

Pulmonic Valvular Disease. Pulmonary insufficiency is classified as congenital and acquired A clinical separation of these two classes of pulmonary valve lesions frequently cannot be made in the adult.

Functional or relative pulmonic insufficiency occurs as the result of a high pressure in the pulmonary artery. The commonest cause of organic pulmonary insufficiency is pulmonary emphysema and rarely bacterial endocarditis involving the pulmonic valve. Bacterial endocarditis of the pulmonic valve is usually not accompanied by other valvular lesions

In pulmonic insufficiency there is dilatation of the pulmonary artery, hypertrophy of the right ventricle with regurgitation of blood from the pulmonary artery

The symptoms of pulmonic insufficiency are always dominated by those of the primary disease Dyspnea and cyanosis may be intense. Polycythemia is observed in the cyanotic patients, and hemoptysis is frequent.

Examination reveals the findings of the primary disease. There may be a Graham Steell murmur in the second or third left interspace in the presence of mitral stenosis and accentuation of the second pulmonic sound

Roentgenologic examination discloses evidence of right ventricular hypertrophy and often a dilatation of the pulmonary artery.

The diagnosis is rarely made clinically.

Cor Pulmonale. Hypertrophy of the right ventricle of the heart, or cor pulmonale, occurs in acute, subacute or chronic form The acute form is commonly caused by large pulmonary emboli The subacute form frequently is due to metastatic carcinomatous infiltration of the perivascular lymphatics and of the pulmonary arterioles; occasionally the subacute lesion follows embolism of the smaller pulmonary vessels. Similar changes in the right ventricle have been found in sickle cell anemia attended by multiple dissemi-

nated thromboses of the smaller pulmonary arteries. Chronic cor pulmonale is often associated with enlargement of the right side of the heart in association with chronic obstructive emphysema, silicosis, bronchiectasis, tuberculosis, bronchial asthma, silicotuberculosis, kyphoscoliosis and pulmonary arteriolar sclerosis In silicosis and bronchiectasis cor pulmonale occurs oftenest in association with peribronchial and perivascular fibrosis rather than with the nodular fibroses In tuberculosis the changes in the right ventricle usually follow extensive sclerotic lesions in the lungs Thoracic deformities, kyphoscoliosis and secondary emphysema seem to be factors in the production of pulmonary hypertension and hypertrophy of the right ventricle. Pressure by tumor on the main pulmonary artery, organized vascular thrombi, schistosomiasis with parasitic invasion of the walls of the pulmonary vessels and diminution in the caliber of the vascular channels lead to increased resistance to the flow of blood and hypertrophy of the right ventricle

A congenital or acquired cardiac lesion with arteriovenous fistulae may cause pulmonary congestion and hypertension

Cor Pulmonale Due to Pulmonary Emphysema (*Emphysema Heart*). Arteriosclerotic changes in the larger pulmonary arteries as well as in the small arteries and arterioles of patients who have advanced emphysema are more frequent and more severe than in normal persons of similar age

Advanced pulmonary emphysema with considerable arterial oxygen unsaturation requires a greater cardiac output In response to the anoxemic stimulus to the bone marrow there is a development of polycythemia, which is an attempt to restore the normal hemoglobin content of oxygen despite the diminution in percentage of oxygen saturation

When virulent bronchopulmonary infection complicates pulmonary emphysema, there is inadequate oxygenation of tissue and right ventricular strain and failure ensue. Bronchial asthma causes cor pulmonale indirectly by first producing an obstructive emphysema Pulmonary tuberculosis of an advanced degree, like obstructive emphysema, may produce both right ventricular hypertrophy and congestive heart failure.

Hypertrophy and dilatation of the right ventricle are present in those who have severe kyphoscoliosis The significant type of kyphoscoliosis is situated in the lower cervical and upper thoracic regions or in the midthoracic region, with the curvature convex to the right. Men are predominantly affected In most cases the cause of kyphoscoliosis is hereditary and congenital However, tuberculosis of the spinal column, rickets, poliomyelitis and osteoarthritis are the causative agents in a great many cases

In kyphoscoliosis in either the congenital or acquired form the thoracic cavity is shortened, the diaphragm elevated, and the volume of the thoracic cavity and consequently of the lungs is diminished The lung on the side of the deformity is compressed, atelectatic, and eventually becomes fibrotic

Symptoms. Rarely are the symptoms of sufficient distinctiveness to cause more than a suspicion of chronic cor pulmonale. Pulmonary emphysema exists as such with or without complications A progression of the disease is complicated by bronchitis or asthma or both A pulmonary circulatory insufficiency may exist in a compensated stage from the time of inception of the emphysema

During the compensated stage of pulmonary heart disease from emphysema there are symptoms of pulmonary hypertension in addition to those of asthma The exertional dyspnea of emphysema is more marked and there may be dyspnea at rest. Occasionally cyanosis is intense and associated with polycythemia. In the decompensated stage of pulmonary heart disease, dyspnea, cyanosis, fainting, vertigo, somnolence and occasionally precordial pain are present.

Examination Pulmonary hypertension may be suspected from accentuation of the second pulmonic sound, and right ventricular hypertrophy suspected from a prominent impulse in the epigastrium. There may be roentgenologic evidence of dilatation of the pulmonary arteries and of the right ventricle.

When there is a *decompensated stage of pulmonary heart disease*, the dyspnea

and cyanosis are intensified Associated with intense cyanosis are polycythemia, hepatic enlargement, systemic venous congestion and peripheral edema Peripheral edema and occasionally ascites are present

The circulation time is normal in uncomplicated pulmonary emphysema, even during an attack of bronchial asthma, and it remains normal during the compensated stage of chronic cor pulmonale When intrapleural pressure is increased so is the venous pressure

The electrocardiogram of chronic cor pulmonale may not disclose any abnormality, or it may reveal the changes due to a vertical position of the heart, depression of the diaphragm and right ventricular strain.

DIAGNOSIS The diagnosis of pulmonary heart disease is more definite when right-sided heart failure is associated with primary pulmonary disease. Hepatic enlargement and subcutaneous edema in addition to elevation in venous pressure are indicative of right ventricular failure.

The history and the results of physical and roentgenologic examinations of the thorax will usually reveal the presence and nature of the pulmonary disease and exclude primary cardiovalvular disease The diagnosis of compensated cor pulmonale requires demonstration of right ventricular enlargement indicated by the roentgenologic examination

DISEASES OF THE HEART DUE TO DISTURBANCES OF INNERVATION OR PSYCHIC CONTROL

Neurocirculatory Asthenia or Cardiac Neurosis. This condition is known also as irritable heart, disordered action of the heart, and effort syndrome.

Neurocirculatory asthenia is a syndrome of psychogenic or neurogenic origin simulating organic heart disease, from which it often cannot be differentiated immediately There are complaints of dyspnea, precordial pain, palpitation and exhaustion

These patients often give a history of "nervous breakdowns," indecision, prolonged illnesses and an intolerance for the vicissitudes of daily life This disorder, however, may occur in any person if there is imposed a sufficient amount of exhaustion and emotional trauma

Neurocirculatory asthenia may occur at any age in persons of either sex, but it seems to be commonest in young men, The hereditary and environmental factors may be important A similarity of somatic type of those who have the disorder is often noticeable. They are of an asthenic build with a long and narrow thorax

In some of those who have neurocirculatory asthenia a serious illness has occasioned a long withdrawal from physical exercise Incident to the withdrawal there was time in which anxieties in regard to ultimate recovery seized the patient. With subsequent illnesses the anxiety and prolongation of disability tend to recur In some patients the anxiety will recur in the absence of other illnesses

SYMPTOMS These patients complain of difficulty in breathing, precordial discomfort, palpitation, vertigo, hyperhidrosis, weakness, gastrointestinal disturbances and often headache On questioning, it will be found that they are fearful of some indescribable danger and impending illness In addition to these complaints it will soon be evident these patients are irritable, restless and unable to sleep. There are present anorexia, slowed processes of thought, and feelings of confusion

A characteristic shortening of breath, described as an inability to take a deep breath, occurs while at rest or during exercise The severity of the dyspnea is disproportionate to the degree of exercise and to the objective disturbances in ventilation

Fatigability, a sense of profound fatigue during the early morning hours and, in some, great exhaustion follow physical exertion. A cardiac disorder which confines a patient to rest in bed for 2 or more months without stirring around is usually neurocirculatory asthenia

Spontaneous attacks of dyspnea, deep breathing and tachypnea, often in association with claustrophobia, occur. Excessive hyperventilation causes giddiness or dizziness and sweating and produces tetany.

Pain in the precordium may be a dull, continuous ache or soreness or may be sharp and intermittent The pain is unrelated to exercise. It occurs at any time during or after meals and exertion If the pain occurs during activity, it is not immediately relieved by rest.

Palpitation may be the first symptom There is an awareness of the heart beat actually associated with tachycardia and a forceful cardiac pulsation. Paroxysms of tachycardia are common

EXAMINATION On examination there will be present cold moist hands and feet. The mouth and lips are dry The pulse rate and the blood pressure are variable, but response to graduated exercise tests is normal It is in these patients that exercise tests and occasionally the anoxia test find their most precise diagnostic applicability. There is a general tenseness of musculature, and hyperactive tendon reflexes are present. Tenderness on pressure to the body by the examining thumb will be complained of wherever the thumb applies pressure

Examination of the heart reveals no constant signs of organic heart disease However, the discovery of organic heart disease which has been unknown to the patient may precipitate the symptoms of neurocirculatory asthenia The heart is normal in size The pulse rate is increased

DIAGNOSIS The functional cardiac and circulatory disorder is indicated by the history, and the lack of objective manifestations of cardiac and circulatory dysfunction These objective findings are evaluated, and separately recorded and if there are no history, symptoms and findings other than the cardiac neurosis a diagnosis of neurocirculatory asthenia is made. If there are symptoms and signs of organic heart disease, in addition to those of the cardiac neurosis the proper diagnosis of cardiac disease and neurocirculatory asthenia is made

THE MYOCARDIUM

The Enlarged Heart. Cardiac enlargement is indicative of the presence of cardiac disease. However, an enlarged heart is often found when no definite evidence of disease which has caused the enlargement is demonstrable Confirmation of suspected cardiac enlargement depends on physical and roentgenologic examinations The presence of cardiac enlargement may be suggested or confirmed by the electrocardiographic findings The past history is important.

ETIOLOGY The commonest causes giving rise to enlargement of the heart are hypertension of the essential type and valvular disease of rheumatic or syphilitic origin

Less common causes of cardiac enlargement than hypertension and valvular disease are myocarditis, cardiac infarction, thyrotoxicosis, chronic pulmonary disease, and congenital defects Rare causes are arteriovenous aneurysms, severe anemia, beriberi, hypothyroidism, thoracic and spinal deformities, chronic pericarditis with external adhesions, and cardiac neoplasms Prolonged physical strain, as in athletic sports, and excessive tachycardia and certain arrhythmias may produce some permanent cardiac enlargement Finally, cardiac enlargement may occur from unknown cause

Age Cardiac enlargement may occur at any age In young persons it is almost always the result of acute rheumatic myocarditis or chronic rheumatic valvular disease, in middle age it is due most often to hypertension but also frequently to chronic valvular disease of rheumatic or syphilitic origin and to myocardial infarction, and sometimes to extensive pulmonary fibrosis In old age it is due chiefly to hypertension, to myocardial infarction and pulmonary emphysema

Sex. Cardiac enlargement is common in both sexes, but the largest hearts (aortic regurgitation of syphilitic aortitis) are commoner in men than in women

PATHOLOGY Cardiac enlargement consists usually of hypertrophy of muscle and dilatation of the chambers It may begin as either one and continue preponderantly as hypertrophy or as dilatation.

Hypertrophy consists in the increase in size of the individual muscle fibers and not in their increase in number. Increase in bulk and weight of the myocardium commonly follows considerably increased work if long sustained The heart is made up of masses of muscle continuous between the ventricles and between the auricles respectively, but hypertrophy and enlargement may be limited to a single part (or parts), as in the case of left ventricular hypertrophy in hypertension and of right ventricular hypertrophy in stenosis of the pulmonary valve.

Dilatation of the heart frequently occurs along with hypertrophy as a part of cardiac enlargement. It consists of a stretching of the heart muscle due to a response to excessive physiologic demand for an increased output of blood per beat. Dilatation may persist or increase with continuance of the demand, the tone of the muscle may partly recover but a permanent stretching of the fibers may persist In some instances enlargement of the heart due preponderantly to dilatation may decrease However, this is not the usual experience with cardiac enlargement, which changes little, tending gradually to increase in the course of time

The largest hearts and the heaviest hearts are those in which *hypertrophy* and *dilatation* are associated The heart is so large that it reaches almost to the thoracic wall on the left and considerably more than halfway to the thoracic wall on the right

Examination in Cardiac Enlargement. The evidences of cardiac enlargement are variable and may be inconclusive unless the heart is definitely enlarged The apex beat may be displaced laterally and downward Often cardiac enlargement is present when the maximal apical impulse is situated lateral to the midclavicular line, or more than 4 inches (about 10 cm) from the midsternal line in the fifth left intercostal space, or below the level of the fifth intercostal space Cardiac displacement due to bronchopulmonary lesions may similarly affect the position of the apical impulse In many persons it is difficult or impossible either to see or clearly to feel the apex beat.

An accentuated or diffuse apical impulse may be present in cardiac enlargement. A precordial bulge is often observed in children with cardiac enlargement due to rheumatic or congenital cardiac disease

On percussion of the adult thorax, if cardiac dullness extends beyond 4 inches (about 10 cm) to the left of the midsternal line in the fifth interspace and there is deformity of the thorax, cardiac enlargement is likely to be present. If cardiac dullness extends more than 1⅗ inches (4 cm) from the midsternal line in the third left interspace, there is probably enlargement of the left atrium, dilatation of the pulmonary artery or enlargement of the pulmonary conus of the right ventricle. The accuracy with which the degree of cardiac enlargement can be discovered by percussion is impaired in obese individuals, in those with muscular thoracic walls, in those who have pulmonary emphysema and in women with large breasts Percussion is limited in the accuracy with which the size of the heart can be determined in the normal thorax without any handicaps unless the heart is definitely enlarged However, relatively few of the total number of patients ill with serious heart disease at home can be moved in order to have more refined methods of diagnosis Indeed, these patients should not be moved for study, and under these circumstances the approximations of the size of the heart by physical examination must suffice. It is for this reason that skill in physical examination is helpful

Diagnosis of Enlarged Heart *Roentgenologic Examination of the Heart* Roentgenologic examination of the heart is the most reliable method of determining cardiac enlargement Friedberg has commented that the roentgenologic examination reveals also the volume of the heart and its vascular extensions and the relative size of the individual chambers Rotating the patient enables viewing the heart from different angles

The size of the heart and the presence and localization of cardiac enlargement may be determined by fluoroscopic, orthodiagraphic and teleroentgenographic examinations In special instances, in cases of congenital heart disease and in dis-

tinguishing cardiac enlargement from extracardiac masses, angiocardiographic and electrokymographic examinations may aid in distinguishing cardiac enlargement from pericardial effusion and ventricular aneurysm

The Normal Cardiac Outlines on Roentgenograms Roentgenologists employ three standard views which yield the maximal information as to the shape, size and (by fluoroscopy) the pulsations of the heart. These views are the anteroposterior, the right oblique anterior and the left oblique anterior

In the *anteroposterior view* the *right border* is composed of the contours, which from above downward are, in young individuals, the innominate vein and its continuation into the superior vena cava In older individuals, the ascending aorta may overshadow the superior vena cava In all, the right atrium is the largest salient of the right border of the heart and it comprises the entire right border except for the superior vena cava or the ascending aorta

The *left border* is formed from above downward by the aortic arch continuing into the descending aorta Then follows the pulmonary salient composed of the pulmonary artery and its left main branch. The left ventricle forms the prominent convex contour which curves downward and back toward the midline

The Transverse Diameter The most informative measurement obtained from teleroentgenograms or orthodiagrams is that of the transverse diameter In the erect position of the body the transverse diameter averages between 4 and 5 inches (about 10 and 13 cm) but even greater variations occur normally

The *cardiothoracic ratio* is employed as an index of cardiac enlargement. This is the ratio of the transverse diameter of the heart to the internal diameter of the thorax at its widest point just above the level of the dome of the diaphragm If the cardiothoracic ratio significantly exceeds 50 per cent it is assumed there is cardiac enlargement This is only a rough guide since the relationship varies considerably. Despite the fact that this is only an approximation in practice, it is of great value

The factors which modify the normal cardiac shadow on the roentgenogram are the somatic types For instance, in a short, broad, rounded thorax the cardiac shadow tends to be short, wide and situated transversely, and the apex appears to be displaced to the left The transverse positions of the heart which affect the cardiothoracic ratio and thus suggest left ventricular enlargement result from elevation of the diaphragm, for example, deep expiration In the presence of hepatic enlargement and ascites, during pregnancy and in obese subjects or a stomach distended with gas, the diaphragm and the heart may be displaced upward and the heart thus displaced may appear to be enlarged Scoliosis, even the slight scoliosis commonly seen in children, produces an apparent enlargement of the cardiac shadow if the heart lies to the left of the spinal column A similar effect is produced by widened rib margins in instances of severe rickets A vertical cardiac shadow may occur in the presence of pulmonary emphysema

The Right Anterior Oblique View The patient is rotated anteriorly so that the right shoulder is turned toward the screen The angle formed by the shoulders with the screen should be about 30 to 40 degrees for study of the aorta, 50 to 60 degrees for study of the left atrium The *anterior border* of the cardiac shadow in this position is formed in its upper third by the ascending aorta and arch, and in its lower two thirds by the pulmonary artery and right ventricle The left ventricle forms the lower border on the roentgenogram

The *posterior border* of the cardiovascular shadow, reading from above downward, first is the outline of the right branch of the pulmonary artery and the superior vena cava The descending aorta may be distinguishable The left atrium forms the slightly convex major portion of the posterior cardiac shadow on the roentgenogram The right atrium with the shadow of the inferior vena cava entering it completes the circumference of the posterior cardiac shadow in this position

The Left Anterior Oblique View The patient is rotated anteriorly so that the left shoulder is toward the screen, a position which the right shoulder occupied in the right anterior oblique view. The *anterior border* of the cardiovascular silhouette in this

position, reading from above downward, first is the innominate vein and superior vena cava. The ascending aorta and the right atrium complete the outline

Reading from above downward the upper third of the *dorsal aspect* is formed by the left atrium, and the lower two thirds is the shadow of the left ventricle

Enlargement of the Individual Cardiac Chambers. Advanced enlargement of the heart often involves the entire heart. *Diffuse enlargement of the heart occurs in* various toxic, infectious, and metabolic diseases, for instance, beriberi, severe anemias, and combined left-sided and right-sided heart failure In some of the most important forms of cardiac disease the cardiac enlargement is confined to one or more chambers. Thus the determination of such localized enlargements is of great diagnostic value.

Left Ventricle Early enlargement of the left ventricle is not revealed roentgenoscopically Moderate left ventricular hypertrophy with minimal dilatation, as seen in essential hypertension, is characterized by rounding of the left lower contour of the heart without alteration in cardiac diameters.

In normal individuals apparent enlargement of the left ventricle is usually due to a high diaphragm. Displacement laterally of the left lower cardiac contour may be caused by enlargement of the right ventricle.

Left Atrium Enlargement of the left atrium may cause a straightening of the left border or a prominence situated in the middle of the shadow Often an enlargement of the left atrium is indicated by compression of the esophagus When extreme enlargement of the left atrium is present, the entire right cardiac border is formed by that chamber

Right Ventricle Enlargement of the right ventricle cannot be detected in its early stages. When the right ventricle is greatly enlarged it forms the entire right border of the cardiac shadow.

Right Atrium Enlargement of the right atrium is revealed in the anteroposterior view by lateral displacement of the right lower cardiac shadow beyond the right midclavicular line Enlargement of the right atrium only occurs in generalized cardiac enlargement

Electrocardiographic Evidence of Cardiac Enlargement Alterations in the size and form of the heart alter the form of the electrocardiogram It is desirable, if possible, to differentiate the electrocardiographic changes due to cardiac enlargement from those caused by the position or rotation of the heart within the thorax incident to somatic type of the individual.

The axis deviations in the conventional leads I, II and III have a relationship to the enlargements of the left or the right chambers of the heart The axis deviations are related to the variations of the height or depth of the R and the S waves in the electrocardiogram The higher the R waves are in lead I and the deeper the S waves are in lead III, the greater is the degree of left axis deviation The higher the R waves in lead III and the deeper the S waves in lead I, the greater is the degree of right axis deviation

It is well to realize that left and right ventricular enlargement are common causes of left or right axis deviation, but axis deviations may be observed in the absence of cardiac enlargement Right axis deviation may be observed in a heart with left ventricular enlargement.

The electrocardiogram indicative of left axis deviation may be observed in some asthenic persons who have a transversely situated heart, in the obese, or in those with high diaphragm due to ascites or pregnancy. A deep expiration increases the degree of the left axis deviation in the electrocardiogram

The electrocardiogram indicative of right axis deviation may be present in asthenic persons who have centrally situated vertical or drop heart and in those who have pulmonary emphysema and low diaphragm. A deep inspiration and the upright position increase the degree of the right axis deviation Right axis deviation may

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The Left Anterior Oblique View. The patient is rotated anteriorly so that the left shoulder is toward the screen, a position which the right shoulder occupied in the right anterior oblique view. The *anterior border* of the cardiovascular silhouette in this

may, like the stroke volume, be reduced but usually to a less degree, since an increase of pulse rate tends to compensate for a decreased output per beat. The erect posture has been found usually to cause a decrease of one fourth to one third of the minute volume calculated for the recumbent position There are other factors which influence blood flow

The normal cardiac output per beat varies in the average adult from 50 to 100 ml. at rest There is an increase of output on exercise which is less in those not accustomed to exercise than it is in those who regularly have physical exercise. In heart failure or extreme tachycardia the cardiac output may be reduced In paroxysmal tachycardia, for example, the cardiac output may be greatly reduced

The speed of flow from arm vein to heart and through heart and lungs to arm artery can be determined The value for this rate of blood flow is termed the circulation rate. Normally this arm to arm circulation time varies from 14 to 24 seconds (average 18 seconds). The arm to arm circulation time increases with the pulse rate but does not change with blood pressure variations, and it is not affected by valvular heart disease The *circulation rate* is decreased in auricular fibrillation and in congestive heart failure. The decrease in congestive heart failure is in accordance with the degree of failure

In the determination of the arm to lung time, that is, the integrity of the venous systemic circulation and the right heart, ether is injected intravenously (using 5 minims of ether and 5 minims of physiologic saline solution); the end point is detected by the patient's consciousness of the presence of ether on the breath. The ether arm to lung time varies from 3 to 9 seconds, averaging 5.8 seconds

In the determination of the circulatory rate, that is, the state of the right ventricle, sodium gluconate, saccharin, or cyanide time (normal average 12 to 15 seconds) is used In the determination of the total heart efficiency, the subtraction of the normal time (12 to 15 seconds) from the time observed in the test will give an estimate of the strength or failure of the left ventricle

Acute Nonspecific Myocarditis. Acute nonspecific myocarditis occurs secondarily to many diseases of bacterial or viral origin and also in some conditions of undetermined origin Acute myocarditis has been demonstrated at necropsy in diphtheria, typhoid fever, paratyphoid fever, typhus fever, dysentery, mumps, pneumonia, scarlet fever, meningococcal infection, gonococcic infection, tularemia, streptococcal and pneumococcal meningitis, pyelitis, bronchiectasis, infectious mononucleosis and acute suppurative tonsillitis

The pathologic change in all instances of acute nonspecific myocarditis is characterized by an acute and often focal inflammation of the myocardium. For instance, in septicemia, a suppurative myocarditis, miliary abscesses may be represented by very small visible spots or streaks surrounded by a red zone which contains pus. The myocardium in rheumatic fever and trichinosis with terminal congestive failure may be diffusely affected [illegible]

SYMPTOMS [illegible]
of the general di[illegible]
fever, or an increase of fever if already present, weakness, palpitation, precordial pain and tachycardia Tachycardia out of proportion to the fever is suggestive of myocarditis if not evidence of peripheral circulatory failure due to toxemia.

Patients whose convalescence from acute infection is slow, with profound asthenia after the acute disease has subsided, may have myocarditis. Slight pre-[illegible]
[illegible] occurring
[illegible] of any
[illegible] of the
heart Enfeeblement of the first heart sound may be the first diagnostic implication of a myocarditis The first heart sound may become indistinguishable from the second sound, resulting in an embryocardiac rhythm An apical systolic murmur occurs frequently A gallop rhythm, with or without cardiac enlargement, occurring in the course of an acute infection, in the absence of pre-existing heart disease, suggests myocarditis

be produced by lateral rotation of the body to the left. A bundle-branch block modifies the apparent electric axis.

The QRS interval may be prolonged to 0.10 or 0.11 second. This prolongation may be due to delay in passage of the electric impulse resulting from an increased thickness of left ventricular muscle or to delay caused by elongation or functional depression of the left bundle branch.

Cardiologists believe that unipolar leads provide more reliable evidence for cardiac enlargement than is obtained by the conventional leads.

Tests of Cardiac Function. Exercise Tests. Before an exercise test is employed, it is well to determine what can be learned from questioning the patient in regard to endurance while performing the ordinary daily activities which are required and have been performed without dyspnea or angina pectoris How long and how far can ordinary walking be pursued without dyspnea or pain? Will it be necessary to hurry, lift or run in order to produce dyspnea or pain? These are but examples of the many inquiries which can be made and which will usually reveal the limits of physical activities which can be indulged in without symptoms Answers to these questions will usually make an exercise test unnecessary

If an exercise test is employed, it should be simple and designed not to exhaust prematurely a person not in good physical training The test or tests are conducted under the observation of the examiner. Walking, marking time by a hopping or running cadence or mounting a specially constructed two step footstool a given number of times within definite time limits are the best tests The test performed with the two step footstool is known as the two step test

In normal persons the blood pressure and pulse return to within 10 of resting levels in one and one-half minutes after a standardized exercise test The more vigorous the exercise, the more slowly do blood pressure and pulse rate return to resting levels In coronary heart disease exercise may cause typical pain

Exercise tests may be of value in detecting coronary insufficiency when it is latent. There is a lag in return of the blood pressure and pulse rate to former levels. The electrocardiogram gives evidence of anoxemia of the heart muscle following exercise ST segment depression or elevation of 1 mm or more in lead I, of 1.5 mm. or more in lead II and lead III and 2 mm. or more in lead IV; and the conversion of T wave in I, II, or IV indicate an insufficient coronary circulation. Likewise the development of bundle branch block is a positive test.

Miscellaneous Tests There are two tests of cardiac function which utilize the respiratory system, namely, determination of vital capacity, and the anoxemia test. The anoxemia test is a special respiratory test which may be of value if performed by those trained to perform it correctly.

The *vital capacity* of the lungs is the measurement, by spirometer, of the amount of air, in liters, that can be expelled by a complete forceful expiration after the fullest possible inspiration (see Diseases of the Lungs, Chapter 9)

There are two primary heart conditions, namely, mitral stenosis and congestive heart failure, which give rise to reductions of vital capacity Pulmonary emphysema, *no matter what may produce it fundamentally*, is also an occasional cause of reduction of the vital capacity

The *anoxemia test* is designed to test the functional capacity of the coronary circulation, especially in persons suspected of having coronary heart disease but without definitely diagnosable angina pectoris or electrocardiographic abnormalities The test is not entirely safe and is less frequently employed than in former times

The determination of the blood flow through the chambers of the heart is dependent on methods utilizing the absorption of such gases as nitrous oxide, ethylene, and ethyl iodide, and acetylene from the lungs in a certain definite time. The time unit is one minute. The volume of *blood expelled from the heart in one minute* which is available to absorb gas is termed the minute volume

The *minute volume* normally ranges from about 3,500 to 9,000 ml (*6 to 12 ml per* [illegible]), being increased by exercise to as high as 20 to 25 liters. It

Electrocardiographic changes may consist of depression of the ST segment and lowering or inversion of T wave, heart block or bundle-branch block.

DIAGNOSIS The presence of acute myocarditis in a patient who has diphtheria is manifested first by a slowing of the pulse There is an enfeebled first sound at the apex, and a gallop rhythm The heart is enlarged. During the second or third week of the disease a severe myocarditis is revealed by the development of congestive heart failure. Electrocardiographic abnormalities consist mainly of a bundle-branch block

Acute myocarditis is a serious complication of diphtheria, accounting for most of the deaths in this disease after the first week

Syphilitic Myocarditis. Primary syphilitic myocarditis is uncommon and is confined to gummatous lesions Gummas situated in the interventricular septum may involve the bundle of His or one of its branches and thus interfere with cardiac rhythm. A gumma may result in cardiac aneurysm, may lead to rupture of a papillary muscle or of the heart wall, or rarely occludes a valvular orifice.

Cardiac gummas and gummatous myocarditis produce no recognizable clinical symptoms Rarely a gummatous aneurysm may perforate into the pericardium and result in sudden death Gummas in the left ventricle or in the interventricular septum may protrude into the valvular regions, producing a pseudostenosis.

Aneurysm of the Ventricle of the Heart. The majority of ventricular aneurysms arise as a result of infarction following coronary thrombosis despite the fact that aneurysms of the heart are uncommon complications of coronary thrombosis

Aneurysm of the ventricle may occur from abscess of the heart wall, from trauma, from ulcerative lesions of bacterial endocarditis or from congenital defects. Instances of the latter type, however, are rare

The left anterior descending coronary artery is the vessel which most commonly is completely occluded, and aneurysms are therefore most commonly present at the apex or anterior wall of the left ventricle These aneurysms are diffuse bulges, varying in diameter from a few centimeters up to a dilatation almost equal in size to the remainder of the ventricle They are rarely saccular in form The overlying pericardium is densely adherent to the heart

SYMPTOMS There is a history of an attack of coronary occlusion The time interval elapsing between this and the development or recognition of the aneurysm is variable, from a few weeks to several years. Occasionally, there is a history of prolonged precordial pain following the initial episode This is not pain of short duration such as occurs in anginal seizures, but is distress lasting for hours or days

EXAMINATION There may be a forceful, abrupt, localized thrust, often felt at or near the apex The heart sounds are enfeebled out of all proportion to the force of the cardiac impulse Gallop rhythm and indistinct murmurs may be present. The blood pressure is commonly normal or low.

Electrocardiograms are of importance only as they may add to the evidence of myocardial infarction and assist in localizing the lesion in the anterior or posterior part of the ventricle

DIAGNOSIS The diagnosis of ventricular aneurysm is based on the clinical history, the physical examination and the roentgenologic study. Roentgenologic study is by far the most important diagnostically

Metabolic and Nutritional Disturbances of the Myocardium. ***Vitamin B_1 Deficiency—Beriberi Heart.*** Beriberi in the United States may be observed in alcoholism and drug addiction, restriction in food intake, neurotic adherence to food fads, poverty with consequent caloric and vitamin deficiency, and occasionally in diabetes, pregnancy and severe gastrointestinal disease.

As part of the *pathologic changes* in beriberi the heart may be normal in size or enlarged Heart failure in beriberi is considered to be the consequence of a thiamine-deficient metabolism of the heart muscle

Acute severe infection associated with toxemia causes peripheral circulatory failure without any significant damage to the myocardium. However, there are alterations of the electrocardiogram which may occur in the course of many acute and occasionally in chronic infectious diseases. These changes are recognized as important in rheumatic disease In the course of acute rheumatic fever or other infections the electrocardiographic changes may return to normal The clinical interpretation is that the pathologic process responsible for the change has resolved without leaving permanent damage to the myocardium.

Congestive heart failure occurs rarely as the result of myocarditis alone. If congestive heart failure occurs during an acute infection, the patient has had a pre-existing heart disease.

DIAGNOSIS The diagnosis of myocarditis can be made correctly and more frequently if it is realized that acute myocarditis is not a rare complication of infectious disease In the experience of Candel and Wheelock clinical evidence of myocarditis was associated with one or more of the following acute infectious diseases peritonsillar abscess, pneumonia, scarlet fever, gonococcic arthritis, cystitis, infectious mononucleosis and typhus fever In addition to the presence of evidence of myocardial strain in a patient who has an acute infectious disease the electrocardiographic alterations may be diagnostically helpful.

Diphtheritic Myocarditis. Acute myocarditis occurs in a few of those who have diphtheria. The incidence is higher in epidemics of severe forms of the disease than in mild forms Myocarditis may complicate cutaneous as well as faucial diphtheria and is often associated with cranial nerve involvement

The circulatory disturbances in those who have diphtheria are due to the action of an exotoxin of the Klebs-Loffler bacillus on the muscle fibers of the heart and vessels. A manifestation of the effects of the exotoxin on the peripheral vessels is the occurrence of shock in some of those who have diphtheria

Fahr described three types of change in the heart. (1) fatty degeneration, (2) myolysis, and (3) interstitial inflammation.

SYMPTOMS. There are both early and late symptoms of acute diphtheritic myocarditis The early symptoms occur near the end of the first week and during the second week In those who have cutaneous diphtheria the heart symptoms may be delayed and begin after 4 to 7 weeks In either instance there are cough and cyanosis which it seems reasonable to attribute to obstruction of the respiratory passages However, those who have a diphtheritic myocarditis, and who have cough and cyanosis, may not have obstruction to the respiratory passages. The cardiac symptoms are often first those of cardiac shock which in rare instances is followed by congestive heart failure

EXAMINATION Tachycardia is usually present in the first week of diphtheria even when there is no demonstrable myocardial involvement. With the development of acute myocarditis there is often a gradual or sharp reduction in the heart rate which may result in a mild or pronounced bradycardia In the third week of the disease tachycardia reappears in those who have myocarditis. Cardiac rates of less than 40 indicate the presence of complete heart block, but the latter may be associated with a normal heart rate or a slight tachycardia Gallop rhythm is an important sign of [illegible] myocarditis with extensive myocardial damage and heart failure Occa- [illegible] nt of the first heart sound, embryo-

Patients who have complete heart block rarely suffer from epileptiform convulsions, syncope or other symptoms of the Adams-Stokes syndrome During the convalescent period, about the fourth to sixth week, patients may present a persistent tachycardia, or a tachycardia induced by slight effort or occurring at the end of the day. A bacterial (diphtheritic) endocarditis due to the Klebs-Löffler bacillus occurs rarely.

Subjective symptoms referable to the heart consist of angina pectoris or complaints due to congestive heart failure. Angina pectoris is due to severe coronary arteriosclerosis which often accompanies myxedema It often is not present until after the administration of thyroid and the elevation of the basal metabolic rate

On examination there are signs associated with advanced myxedema which are similar to those of congestive heart failure. Thus there are peripheral edemas, ascites, pleural effusion and hydropericardium which have not responded to digitalis or diuretics The skin is cool and dry. The blood pressure shows no constant or significant change.

The heart is definitely enlarged in advanced myxedema. In some instances the enlargement is apparent only, for there is a pericardial effusion rather than dilatation or hypertrophy of the heart itself. In either case it may be difficult or impossible to feel a precordial pulsation or to localize the apical impulse. The heart sounds are enfeebled

The electrocardiographic changes consist of low voltage of all the complexes, but most frequently of T and P, and flattening or inversion of the T waves An increased voltage of the ventricular complexes follows thyroid therapy.

Myxedema may be recognized at times from the cold, dry, thickened skin, scanty hair and eyebrows, puffy eyelids, and mental and physical sluggishness, constipation and intolerance to cold The basal metabolic rate is usually between —25 and —35 per cent There are cardiac enlargement, low voltage and flattening and inversion of the T waves in the electrocardiogram in patients who have myxedema. Diagnostic confirmation is obtained by restoration of a normal cardiac function on administration of adequate amounts of thyroid.

Radioactive iodine may be employed when the history and the findings on examination are inconclusive for a diagnosis of heart disease resulting from myxedema

Cardiac and Circulatory Decompensation (Congestive Heart Failure). The term congestive heart failure designates a state or a condition which results when the myocardium is unable to perform, or is prevented from performing, its functional tasks The term is not desirable when used to define a diagnosis, but it may be the only diagnostic descriptive term which can be assigned in a particular instance of heart failure and under these circumstances such a diagnosis is acceptable.

The precipitating causes for the onset of congestive heart failure can be determined in about one half of those who have heart failure These causes are infection, inadequate coronary blood flow, changes in rate and rhythm, pregnancy and childbirth, anemia, pulmonary embolism, transfusion of blood and of sodium-containing [illegible] a person who has

[illegible] :ase such as diphtheria, or in cases of multiple coronary occlusions with extensive myocardial fibrosis and infarction, probably is caused by destruction of a sufficient amount of muscle tissue to cause impairment of its contractility to such extent that the heart is unable to maintain the circulation, for, as a rule, the lesions of rheumatic, hypertensive, arteriosclerotic, syphilitic and other forms of heart disease remain essentially the same during heart failure The immediate lack of correlation between the lesions present in the heart and heart failure may be inapparent. However, impending heart failure is manifested by certain reliable criteria which can be recognized Edema is a most important manifestation of myocardial failure and this is a product of deranged sodium excretion Therefore the generally accepted conception of heart failure recognizes the importance of deranged sodium excretion and edema in heart failure but also recognizes the importance of a weakened cardiac muscle.

Clinical manifestations which are considered evidence of myocardial insufficiency have their origin in the failure of heart muscle in ventricular contraction

The cardiac *symptoms* often start with palpitation, fatigue and rapid heart beat Breathlessness and peripheral edema develop early. Progressive dyspnea, orthopnea, attacks of cardiac asthma or pulmonary edema appear. Increasing subcutaneous edema, serous effusions, engorgement of the cervical veins and enlargement of the liver result from failure of the right side of the heart which is added to the existing failure of the left side of the heart. Shock may result from acute cardiac failure or from acute peripheral vasodilatation.

Vitamin B_1 deficiency or beriberi heart disease may be first manifested soon after surgical operation in chronic alcoholics.

Examination reveals an enlarged heart with an enfeebled first heart sound accompanied by systolic murmurs, a gallop rhythm and a fast pulse rate. The blood pressure is normal The superficial veins are engorged. There are the neurologic evidences of beriberi The electrocardiogram may disclose depressed diphasic or inverted T waves. Low voltage of the QRS complexes and a prolongation of the QT interval are present. Roentgenologic examination often reveals cardiac enlargement

The diagnosis of beriberi heart is considered in all cases of unexplained cardiac enlargement or unexplained cardiac failure, particularly in patients less than 45 years of age, and in postoperative heart failure in chronic alcoholics The diagnosis is based on the presence of the cardiovascular abnormalities in association with peripheral neuritis There may also be concomitant signs of pellagra and occasionally of scurvy

The Myocardium in Endocrine Diseases. *Hyperthyroidism.* Kepler and Barnes found organic heart disease in 18 of 27 instances of fatal hyperthyroidism in which there had been evidence of congestive heart failure.

Hyperthyroidism is common between the ages of 20 and 40 years. In contrast, thyroid heart disease before the age of 40 years is not common. In 108 patients who had thyroid heart disease recorded by Barker and others the average age was 51 5 years, an age which seems to antedate the average age for the appearance of hypertensive arteriosclerosis

Women have hyperthyroidism more frequently than men, in a ratio of 5 1 However, men who have hyperthyroidism have heart disease much more frequently.

Thyroid heart disease is often manifested by auricular fibrillation, cardiac enlargement and heart failure Whether or not this so-called thyroid heart disease is the manifestation of a coexistent independent heart disease is often very difficult to determine, for the basal metabolic rate may be equivocal, and too it may be elevated in hypertension Studies of radioactive iodine and protein-bound iodine seem to make the differentiation more precise. The normal heart is capable of adjusting itself for a long time to the requirements imposed by excessive thyroid secretion and increased metabolism However, the added work of hypertension and the diminished cardiac efficiency due to myocardial anoxia may render the heart unable to maintain its normal size and remain compensated

The diagnosis requires first the recognition of the presence of hyperthyroidism This can usually be most quickly done by the determination and proper interpretation of the basal metabolic rate Heart disease associated with hyperthyroidism or adenomatous goiter can often be diagnosed if attempts are made to account for the presence of a paroxysmal or persistent auricular fibrillation of undetermined heart failure without apparent cause, heart failure which does not respond well or at all to digitalis; heart disease with unexplained tachycardia, and the presence of congestive heart failure without arteriosclerosis, rheumatic valvular heart disease, fever, anemia or vitamin B_1 deficiency. In borderline instances of hyperthyroidism, radioactive iodine may be diagnostic if it is properly employed and the results are correctly interpreted (see Diseases of the Thyroid, Chapter 14).

Myxedema. Myxedema is characterized by a reduction in basal metabolism. It

the age of 40 years it usually is due to rheumatic fever. Left ventricular failure after the age of 40 years is generally caused by hypertension, coronary artery disease, aortic valvular disease or rheumatic fever.

Left ventricular failure arises when dilatation and hypertrophy of the left side of the heart cannot maintain an adequate cardiac output. This inability results first in an increased volume and pressure of blood in the left side of the heart followed by a rise of pressure in the pulmonary veins and capillaries

The symptoms of left ventricular failure arise from the engorgement of the lungs. The resulting rigidity and loss of elasticity of the lungs from engorgement interfere with respiratory movements; and a reduction in vital capacity, impairment of diffusion of oxygen and slowing of the pulmonary circulation ensue.

The lungs in left ventricular failure are more solid than normal and dark red in color. In long-standing pulmonary congestion the lung is usually dry, indurated, and brown owing to deposition of hemosiderin (brown induration of the lungs). Pulmonary emboli and infarcts, hemorrhages, hypostatic congestion, bronchopneumonia and bronchitis are concomitants of this form of congestive heart failure.

SYMPTOMS. One of the first symptoms of left ventricular failure is prolongation of breathlessness after exertion which soon becomes dyspnea Dyspnea is respiratory distress associated with increased effort in breathing It is of a panting or puffing quality and not an inability to take a deep breath Cardiac dyspnea is characterized by rapid, shallow respirations, and is precipitated by exertions previously performed without discomfort At first it occurs only with moderately severe exertions.

The excessive work of the muscles of respiration and the use of muscles not ordinarily required in unconscious breathing to distend and deflate the rigid lungs may be causes for the subjective distress of dyspnea which is localized in the upper part of the abdomen, the thoracic wall and the neck.

Paroxysmal dyspnea, paroxysmal nocturnal dyspnea and cardiac asthma are the forms of respiratory distress which appear in attacks during the day and the night. All of these dyspneas are due to pulmonary congestion The term cardiac asthma is employed synonymously with paroxysmal dyspnea because the wheezing character of the respiration and the signs in the lungs resemble those in bronchial asthma. Paroxysmal dyspnea may or may not occur in those suffering from exertional dyspnea and from orthopnea Often a patient is comfortable during the day but becomes distressed by dyspnea at night, or all of the attacks may occur during the day

The attack of nocturnal dyspnea often commences an hour or two after the patient has fallen asleep Cough, bad dreams, recumbent position, and abdominal distention are causative factors in the production of nocturnal dyspnea In the attack the patient awakens with a sense of suffocation Relief from mild attacks is obtained by sitting up, or after coughing up and expectorating thick mucus, often blood-tinged

In severe attacks the distress is intense and prolonged The patient, as during an attack of asthma, sits upright in bed and tries to get more air. The breathing is regular, rapid and often noisy owing to bubbling or gurgling sounds caused by moisture in the lungs The attacks may follow each other in rapid succession if a hypodermic injection of morphine is not administered. The following day the patient may feel well, but more often is exhausted and breathless

During the attacks of cardiac asthma the severity of pulmonary congestion is increased. Rales appear in the lungs or, if rales already are present, they become more extensive The second pulmonic sound becomes more accentuated and may be more distinct than the second aortic sound

Cardiac orthopnea is a symptom of left-sided heart failure and is due, like the various forms of dyspnea, to pulmonary congestion Orthopnea is the form of dyspnea which occurs when the patient assumes a recumbent position There is an increase in pulmonary congestion in the recumbent position, for there is a shift of blood to the thorax from the lower extremities and splanchnic viscera In the re-

adequately to supply the tissues with blood. There is thus a gradual or sudden dropping off of the ability of the heart to continue to increase, absolutely or relatively, the ventricular output in response to the demands.

Apparently the circulation in the kidneys is most sensitive to changes in the general circulation, and renal blood flow is the first to be affected by relative or absolute decrease in cardiac output. The kidneys promptly effect a shift in blood volume flow and secondarily in salt and water metabolism. The urinary output may be reduced to a fifth of normal, and yet there is specifically only sodium retention.

The secondary constriction of the efferent arteries may insure a normal glomerular filtration of sodium but not a normal excretion of sodium since tubular reabsorption of sodium has become supernormal. The kidneys and tissues seem to hold tenaciously to sodium in patients who have congestive failure. The retention of the sodium has been held responsible for the increased blood volume and the rise in venous pressure.

In human beings the larger the heart, the less is its mechanical efficiency. The physicochemical disadvantage of the hypertrophied heart with respect to oxygenation becomes intensified in the presence of tachycardia. For any given cardiac output, the oxygen requirement increases with an increase in cardiac rate. The increase in cardiac rate shortens the diastolic period, during which almost all of the oxygen diffusion occurs.

The theories of heart failure have been based on data obtained from catheterization of the right atrium, right ventricle and pulmonary artery.

The Theory of Backward Pressure Heart Failure. The classic example of congestive or backward pressure heart failure, according to Harrison, and Heyer and Harrison, *develops as the gradient of blood flow between the pulmonary and aortic systems* drops off and as increased blood mass accumulates in the venous channels back of the heart. The rate of accumulation of this blood mass determines the extent and character of the clinical symptoms. In the suddenly developing acute insufficiency extreme dyspnea and orthopnea develop and acute pulmonary edema promptly ensues. In chronic insidious congestive heart failure, besides pulmonary congestion the right ventricle also fails, with ensuing engorgement of the liver and ascites accumulating very late and producing edema in the dependent parts.

Chronic backward failure is the traditional congestive failure, with low cardiac output and low pulse pressure. *It is found in myocarditis of coronary atherosclerotic origin*, myocardial infarction, rheumatic myocarditis, diastolic hypertension, hypothyroidism, heart tamponade and pericardial constriction.

This backward or congestive failure often appears early in rheumatic carditis or coronary insufficiency *while there is still considerable myocardial reserve.*

The Theory of Circulatory Forward Propulsion Failure. In forward, or circulatory, failure there is normal or supernormal yet inadequate performance of the left ventricle. Acute forward circulatory failure occurs in cardiac standstill, extreme bradycardia or tachycardia, shock and hemorrhage. Chronic circulatory forward failure of the type *with high systolic cardiac output and high pulse pressure,* yet insufficient minute volume of blood flow, occurs in rheumatic or syphilitic aortic regurgitations, systolic hypertension, hyperthyroidism, arteriovenous shunt, congenital lesions, anemia and beriberi.

In these conditions the cardiac output in failure has been shown to be normal or [illegible] increased but still inadequate. The minute volume circulation *is not* greatly [illegible] may

C[illegible]

Congestive heart failure may originate from disease of either the [illegible] side of the heart

Failure of the left ventricle of the heart is the commonest and therefore the most important form of congestive heart failure. It always is the result of a failure of the myocardium of the left ventricle to perform its assigned task. When it occurs before

sounds. Gallop rhythm is present only when there is tachycardia. Auricular fibrillation is frequent in all forms of left-sided heart failure but commonest in rheumatic carditis.

Alternation of the pulse may be a sign of left ventricular failure. It is recognized by inflating the cuff to the systolic pressure. As the cuff is very slowly deflated, only alternate beats are heard for a distance of 2 to 10 mm or more of mercury below the systolic level. Rarely pulsus alternans is recognizable by palpation of the radial pulse; unlike premature beats of pulsus bigeminus, the weak beat is very slightly closer to the succeeding beat than to the preceding one. The heart sounds do not usually appear to be modified, but graphic records have demonstrated such alternation in intensity of the sounds Alternation of the QRS or T wave or of any other wave in the electrocardiogram may be associated with pulsus alternans.

The signs of basal rales and emphysema usually are those of a functional emphysema. Between attacks of cardiac asthma or pulmonary edema there may be no rales at the bases of the lungs posteriorly. When rales are present they often are unilateral and predominantly on the right side. During or immediately after an attack of cardiac asthma there may be many sonorous or sibilant rales resembling the rhonchi of bronchial asthma With pulmonary edema, fine and coarse moist rales become more extensive and the entire thorax may be filled with bubbling or gurgling sounds. In addition there may be signs of a complicating bronchitis, bronchiectasis, bronchopneumonia or pulmonary infarction

Hydrothorax in the course of congestive heart failure appears on the right side.

Edema is an important finding in left-sided heart failure Sodium-water retention is a primary prerequisite for the development of edema, but edema is not necessarily a direct consequence of salt-water retention Hypervolemia, increased venous return to an incompetent cardiac chamber, and increased venous pressure are a sequence of events which determine the appearance and localization of edema after renal retention of sodium and water occurs

The reduction in blood proteins in most cases of heart failure is relatively too small to cause edema. Occasionally the blood protein is low enough as in cases of constrictive pericarditis to cause edema Edema occurs when the concentration of serum protein is less than 5 gm per 100 ml (albumin less than 2 5 gm per 100 ml)

Circulatory measurements are altered in left-sided heart failure The circulation time is prolonged The arm-to-tongue time exceeds the upper limit of normal, 16 seconds, and may be 40 seconds or more. The vital capacity is diminished The venous pressure is normal in the absence of concomitant right-sided heart failure.

The basal metabolic rate may be slightly or greatly elevated

Diagnosis. The diagnosis of left-sided heart failure is made on the basis of the symptoms and signs of pulmonary congestion in a person who has the types of cardiac diseases which usually lead to left-sided heart failure.

The diagnosis of left-sided heart failure involves often the distinction of left heart failure from bronchopulmonary disease, as suggested by such symptoms as cough, dyspnea, hemoptysis and asthma Roentgenograms of the thorax and physical and electrocardiographic examination to determine the presence of underlying cardiac disease are helpful The history may provide the diagnostic data that are not otherwise available A prolonged circulation time distinguishes cardiac from bronchial asthma

Congestive Heart Failure Associated With Failure of the Right Ventricle. When the entire myocardium is weakened sufficiently to cause symptoms of heart failure, the weak right ventricle yields first

The primary diseases of the lungs which cause right-sided heart failure are: Disease of pulmonary vessels or of the pulmonic valve causes strain and consequent

cumbent position, the cardiac output and the venous return are augmented The diaphragm is elevated and consequently this interferes with thoracic breathing because of shortening the thoracic compartment available for expansion This mechanical factor is more important in the presence of ascites and enlarged liver and abdominal tympanites. An enlarged liver and ascites elevate the diaphragm as well as interfering with diaphragmatic movements. It is strangely true that in some patients an orthopnea may occur in one recumbent position, for instance, on the left side, but not in another (trepopnea).

Clinical manifestations of pulmonary edema may be observed in patients suffering from cardiac asthma, but it may appear for the first time in a patient while an attack of coronary occlusion is in progress, during a hypertensive crisis, or after transfusions or intravenous infusions

Acute pulmonary edema is manifested by intense dyspnea, orthopnea, cough, extreme anxiety, and noisy gurgling or bubbling sounds Often there is intense precordial oppression or pain There may be a transition of an attack of cardiac asthma into one of pulmonary edema. In severe attacks the patient drowns from the profuse secretions which cannot empty rapidly enough from the nose and mouth The sputum is frothy and pink-stained because of the presence of blood

The patient is cyanotic, the skin is covered by a cold sweat The pulse is full but if relief is not obtained it becomes rapid and weak

The attack of pulmonary edema usually subsides spontaneously after a few minutes or hours, after coughing up of some blood-stained, frothy sputum. The attack may be rapidly controlled by an injection of morphine, the application of tourniquets to the extremities, or a generous venesection While any given attack usually subsides spontaneously or with treatment, acute pulmonary edema may end fatally. In those who recover, temporary exhaustion follows the attack.

Pulmonary edema and cardiac asthma are less frequent in left ventricular failure due to mitral stenosis than in left ventricular failure due to hypertension, despite the presence of long-standing congestion in the former.

Cough commences with the attack of dyspnea and with pulmonary edema in patients who have left-sided heart failure It may be present in the intervals between attacks, it is very likely to be worse at night The cough of heart failure is induced only by exertion or recumbency In elderly patients a cough and bronchitis, without or with mild fever, may have its origin in congestive heart failure.

In mitral stenosis cough is often an important symptom. A cough may have its origin from other causes such as bronchitis or to a large left atrium or pulmonary artery compressing a bronchus, or to a congenital double aortic arch, or from mediastinal tumor

Hemoptysis in mitral stenosis is common, in hypertensive heart failure uncommon It usually is due to congestion of the lungs but it may be associated with pulmonary embolism and infarction

Examination. Enlargement of the heart may be revealed by inspection and palpation of the apical impulse, by percussion and by roentgenologic examination.

The arterial blood pressure may be unchanged, may fall or may become elevated, depending in large measure on the underlying disease and the factors precipitating heart failure.

In left-sided heart failure, accentuation of the second pulmonic sound is due to the high tension in the pulmonary artery The second pulmonic sound may become louder than the second aortic sound even when there is present systemic hypertension.

An apical systolic murmur is frequently present owing to a relative mitral insufficiency. Tachycardia is frequent Ticktack sounds (embryocardia) may result from shortening of diastole by tachycardia with consequent even spacing of the two

EXAMINATION. On examination of one who has right ventricular heart failure, subcutaneous edema and venous congestion are the most definite findings In ambulatory patients the edema may be present in the evening and absent after a night's rest in bed. In a patient who has been in bed for some days or longer, the edema is most prominent over the sacral region. Sometimes there is generalized, massive edema (anasarca) affecting all parts of the body including the genitalia, thoracic wall, arms and face. A considerable amount of fluid may accumulate in the subcutaneous tissues before edema becomes apparent.

Prominence of the superficial veins is an early sign of right-sided heart failure and may be noticeable before there is detectable subcutaneous edema, hepatic enlargement or other signs of heart failure

Cyanosis is almost constantly present in those who have right ventricular heart failure. It may result from a secondary pulmonary disease or a congenital cardiac lesion causing admixture of arterial and venous blood. In most cases of combined right ventricular and left ventricular heart failure, cyanosis is a prominent manifestation.

Cardiac enlargement is present and it is more pronounced than in left heart failure. In those who have right-sided heart failure secondary to intrinsic pulmonary disease the enlargement of the heart is often difficult to demonstrate. The cardiac size is demonstrated with ease in those who have tricuspid insufficiency and stenosis and those who have a constrictive pericarditis with failure.

Hydrothorax is a common finding of right ventricular heart failure. These pleural effusions in right-sided heart failure occur oftenest in the right pleural cavity or are most extensive on that side when there are bilateral effusions

Hepatic enlargement is often present before there is edema and may remain after the edema has disappeared In the presence of severe heart failure, if there is significant tricuspid valvular insufficiency or auricular fibrillation, the liver pulsates synchronously with the right ventricular pulsations Abdominal pressure over the engorged liver causes or increases visible engorgement of the cervical veins and a rise in venous pressure

The large liver may be tender and painful. The urobilinogen in the urine is increased Hyperbilirubinemia is frequently present, but it is not usually sufficient to produce jaundice The van den Bergh reaction is often delayed or indirect. An impairment of hepatic function may be indicated by excessive retention of injected sulfobromophthalein sodium. Ascites is commonly present.

The urine is concentrated and has a high specific gravity. When cardiac edema disappears the specific gravity is low. The specific gravity of the urine remains low if cardiac failure has complicated a renal insufficiency, or after frequent administration of mercurial diuretics, or prolonged and extreme restriction of sodium intake.

The concentration of sodium in the *plasma* is diminished despite the reduction in urinary sodium

The concentration of chloride in the plasma may be normal when the plasma sodium is depressed if there is a low carbon dioxide-combining power and a tendency to acidosis In the presence of renal insufficiency both plasma sodium and chloride are diminished in concentration, with evidence of acidosis due to retention of fixed acids

Slight albuminuria is common in congestive heart failure Hyaline, granular and epithelial casts are present

Moderate *azotemia*, as indicated by urea nitrogen between 20 and 40 mg. per 100 ml of blood, is the rule Hypoproteinemia is rare but may occur after prolonged heart failure from an ensuing malnutrition, impaired hepatic function, and a long-continued loss of albumin in the urine.

The circulation time is prolonged. The blood volume is augmented The venous

failure of the right ventricle (cor pulmonale). Isolated tricuspid stenosis may cause failure of the right atrium and an ensuing failure of the right ventricle Obstruction to the inflow of blood into the right atrium such as constrictive pericarditis and prolonged ectopic tachycardias may lead to right-sided heart failure. Renal retention of sodium and water augments the circulating blood volume and venous return to the right atrium and ventricle. The incompetent right heart is unable to accept and expel this venous return, and blood is dammed up in the systemic veins and capillaries (Friedberg)

PATHOLOGY The lungs are congested. The liver is dark red or brownish, enlarged and firm because of chronic passive congestion In cases of long standing the liver may have undergone atrophy so that it may be smaller than normal. The term nutmeg liver refers to the appearance produced by the alternation of dark red and light brown areas When the process of connective tissue replacement and fibrous retraction is extensive, the changes in the liver are described as cardiac cirrhosis Ascites is common.

There is passive congestion of the spleen, which is enlarged, dark red and firm The pancreas may also be affected by passive congestion. The kidneys are dark red and are firmer than usual. Heart failure does not cause contraction of the kidneys.

The brain is sometimes infarcted and softened

SYMPTOMS The symptoms of right-sided and left-sided heart failure are usually combined, and often they appear simultaneously or so nearly so that clinically the symptoms are the same in both cases except for the general symptoms of the condition which may be the cause of failure of the right side of the heart

The symptoms of right-sided heart failure are largely due to engorgement and elevation in pressure of the systemic veins and capillaries and the associated sodium-water retention

Fever is often present and is due to an associated pulmonary infarction or bronchopneumonia, rheumatic activity, bacterial endocarditis or some other infection. Pain attends the fever and may be helpful in determining its cause.

Weakness is a definite symptom in advanced failure, and is sometimes associated with extreme loss of weight and anemia Excessive treatment administered by mouth and by vein may add to the weakness already present.

Owing to venous engorgement and medications, anorexia and abdominal distention or a sense of fullness after meals is frequent Nausea and vomiting attend the gastric congestion and may be enhanced by excessive use of digitalis, morphine and the enthusiastic use of chemotherapy and antibiotics The combination of meteorism with hepatic enlargement and sometimes also ascites and constipation may cause fecal impaction in the colon or rectum In an occasional instance of right heart failure with fecal impaction a period of observation may be required to be certain colonic obstruction is not present

Nocturia and polyuria are frequently present but these symptoms are not due to heart failure Often they are due to irritation of the bladder or urethra by concentrated urine. Nocturia in men may be due to an enlarged prostate gland In either men or women nocturia may be occasioned by the elimination of occult edematous fluid Oliguria is a characteristic feature of right-sided heart failure. On improvement the volume of urine increases. In some instances of spontaneous or therapeutic diuresis a urinary volume of several liters may be voided in a day.

Headache, insomnia and mental depression may arise if the patient is aware of the serious danger to life that heart failure imparts. Delirium, hallucinations and delusions of a paranoid type and extreme weakness may follow excessive diuresis and loss of sodium chloride Morphine, barbiturates and digitalis may be contributory causes of mental symptoms, for heart failure alone usually does not cause mental symptoms. The loss of potassium may contribute to the production of these symptoms.

Aphasia, paralyses, convulsions and coma may be due to a complicating cerebral infarction.

The painless character of pericarditis in uremia and other terminal diseases is explained by the absence of pleuropericarditis.

Acute Pericarditis. An acute pericarditis comprises acute fibrinous pericarditis and purulent pericarditis

Acute fibrinous pericarditis is usually a part of the pericarditis of acute rheumatic fever. It is characterized by a sterile pericardial effusion The etiology is unknown. The disease occurs in young adults and shortly after a mild infection of the upper part of the respiratory tract. The initial pain, physical findings, and electrocardiographic abnormalities may simulate acute myocardial infarction. The disease subsides spontaneously within a few weeks but occasionally produces an adhesive pericarditis.

The symptoms vary in intensity and consist of pain and, if effusion is present, dyspnea There may be some fever.

On examination a pericardial friction rub is present. A pericardial friction rub may be associated with a dry fibrinous pericarditis or it may be heard in the presence of a pericardial effusion. A pericardial rub is a sign of an acute fibrinous pericarditis, with or without an effusion.

On auscultation a pericardial friction rub is heard as a superficial, scraping, scratchy or grating sound or occasionally one with a coarse squeaking quality, a sound often described as being similar to that of squeaking leather. There are usually to-and-fro sounds, due to vibrations set up during ventricular and auricular systole.

The pericardial rub is heard just to the left of the lower one third of the sternum It is well localized to a small area. The point at which it is best heard may shift with a change in the patient's position The loudness of the rub is intensified if the patient leans forward and moderate pressure is made on the thoracic wall with the stethoscope The pericardial rubs may be audible for only a few hours at a time and intermittently. Occasionally they persist for weeks or even months.

Purulent pericarditis is the commonest form of pericarditis. The causative organisms are usually the staphylococci, the pneumococci and the hemolytic streptococci A variety of other microorganisms are occasionally responsible, including the meningococcus and *Pasteurella tularensis*.

A purulent pericarditis arises by direct extension of an intrathoracic or intra-abdominal infection, by hematogenous bacterial dissemination, or by traumatic introduction of bacteria through the thoracic wall Staphylococcal or streptococcal septicemia and pneumococcal or streptococcal empyema, especially of the left pleural cavity, are commonly associated Bacterial pericarditis, like pleuritis, may be fibrinous at its onset and then serofibrinous or serohemorrhagic before it becomes purulent

Unexplained dyspnea, cyanosis, venous engorgement about the head and neck, falling blood pressure and weak rapid pulse in a patient who is ill from thoracic or abdominal infection or from septicemia and osteomyelitis, may be manifestations of acute pericarditis The prevailing symptoms referable to a pericarditis are dyspnea and pain.

Compression of the trachea, bronchi and lungs caused by the distended pericardium produces dyspnea The respiratory embarrassment may become critical.

Pain is present in only half of the seriously ill patients It is precordial in situation and often extends to the left shoulder and arm, the neck, the epigastrium and the left scapular regions. The pain is intensified by deep inspiration, by movement of the thoracic wall and by cough

On examination the patient is restless, cyanotic or pale, sits up and leans forward and does not want to be annoyed by examinations.

The cardiac impulse is weak or absent The heart sounds are enfeebled. In some instances the apical impulses and heart beats remain visible, palpable and audible in the presence of massive effusions.

pressure is elevated in contrast with the normal venous pressure in failure of the left ventricle. The arterial blood pressure undergoes no characteristic change

DIAGNOSIS. The diagnosis of right-sided heart failure in those known to have left-sided heart failure is made easily by the appearance of the combination of congested cervical and peripheral veins, subcutaneous edema of the dependent parts, and hepatic enlargement. Right heart failure is easily diagnosed in those who have primary disease of the lungs. A severe reaction following the intravenous infusion of isotonic saline solution and characterized by evidences of an increased venous pressure may be the first indication of right-sided heart failure in a patient who has left-sided heart failure or a weak myocardium.

The *course* of congestive heart failure is often determined or modified by the underlying cardiac disease.

In most reports of studies on *prognosis* in heart failure it is stated that the duration of life in cardiac disease complicated by right heart failure is usually 1 to 2 years, rarely is it 5 years

In general, the prognosis is relatively favorable if the symptoms of congestive failure subside rapidly and completely with appropriate treatment.

The prognosis in any particular instance of congestive heart failure should be guarded even when it appears relatively favorable, because of the danger of serious complications or sudden death.

THE PERICARDIUM

The pericardium is composed of fibrous tissue lined with serous membrane.

The pericardium is somewhat conical in shape Its base rests on the central tendon of the diaphragm, and its apex envelops the great vessels, as they emerge from the base of the heart, for a distance of 1⅔ to 2 inches (about 4 to 5 cm) The attachment to the diaphragm is firmest at the opening of the inferior vena cava As the fibrous layer of the pericardium proceeds upward, it becomes lost in the fibrous tissue (sheath) covering the great vessels. This is continuous above with the deep cervical fascia, especially with its pretracheal layer.

On each side the pleura and the pericardium are in contact, with the phrenic nerve and its accompanying vessels between them. Posteriorly the pericardium lies on the bronchi, the esophagus, and the thoracic aorta

Owing to its fibrous nature, the pericardium will not expand rapidly. When a pericardial effusion attains a large size it creates an increased mediastinal pressure and causes circulatory symptoms by obstruction of the circulation at the base of the heart; respiratory symptoms by pressure on the bronchi; and digestive symptoms from pressure on the esophagus and displacement of the stomach and liver downward. There are alterations in or loss of the voice from pressure on the recurrent left laryngeal nerve (see Mediastinal Tumors, Chapter 9).

Pericardiac Pain. Paracentesis of the pericardium at the level of the fifth and sixth interspaces near the mammary line elicits pain, sharp and restricted to a point over the trapezius ridge. Penetration of the pericardium at higher levels does not produce pain. This pain is similar to that caused by irritation of the central portion of the diaphragmatic pleura It is therefore evidence that the phrenic nerve endings are reflected over the lower portion of the fibrous pericardium

According to Capps scratching or pressure on the heart itself produces no pain The inner surface or serous layer of the pericardium gives no pain response to irritation

When pain is present with an acute fibrinous pericarditis, it is due to involvement of the pleuropericardial surfaces, if the pleura anterior or posterior to the sac is affected, the pain is sternal or posterior, if the diaphragmatic pleura is inflamed, the pain is referred to the neck or to the abdomen. This pain is nearly always excited by cough, deep breath or change of posture.

In heavy infection the cardiac symptoms and findings resemble those of beriberi. There are edema, dilatation of the heart and congestive heart failure The cerebral symptoms are those of cerebral hemorrhage or thrombosis.

The diagnosis is established by finding the characteristic ova in the feces in association with heart failure otherwise unexplained. The ova of *Clonorchis sinensis*, various species of *Opisthorchis, Heterophyes heterophyes,* and other heterophyid flukes resemble those of *Metagonimus yokogawai*.

TUMORS OF THE HEART

Tumors of the heart and pericardium are relatively unimportant as a cause of clinical heart disease. These tumors occur in either benign or malignant forms The benign tumors are myxoma, rhabdomyoma, fibroma, lipoma, angioma, papilloma, teratoma, leiomyoma, and xanthoma The malignant tumors occur as sarcoma, mesothelioma or mesothelial sarcoma of the pericardium, rhabdomyosarcoma, and epicardial epitheliomas.

Secondary malignant tumors which are occasionally present are carcinoma and sarcoma by direct invasion or sarcoma by metastasis

Hodgkin's disease, lymphosarcoma, leukemia and Kaposi's sarcoma may affect the heart

SYMPTOMS Most cardiac tumors do not produce clinical symptoms and are discovered only at postmortem examination.

Symptoms of congestive heart failure are generally regarded as the commonest manifestations of cardiac neoplasms. The heart failure due to cardiac tumors is characterized by its sudden and unexplained development, intractability, rapidly progressive course and its failure to respond to therapy

The Superior Caval Syndrome. The superior caval syndrome results from lymphomatous, metastatic or primary malignant neoplasms of the pericardium The onset is often with cough, malaise and fever Later the full clinical syndrome develops which consists of increasing dyspnea, engorgement of the cervical veins, enlargement of the liver, and small rapid pulse

DIAGNOSIS Occasionally a correct antemortem diagnosis of secondary (malignant) tumors of the heart is made Primary tumors also have been recognized during life.

The diagnosis depends on alert awareness that cardiac neoplasm may be responsible for cardiac manifestations, especially when the clinical course is atypical. In the presence of a malignant neoplasm elsewhere in the body, especially in the neighboring thoracic organs, the onset of rapid heart failure is significant.

CONGENITAL HEART DISEASE

Heart disease prior to the age of 5 years is usually of congenital origin. In older children who have heart ailments, the disorder in about 1 in every 10 is congenital. Among adults congenital heart disease accounts for an insignificant part of the total who are disabled from heart disease

The incidence of congenital heart disease is equally divided between the sexes

ETIOLOGY In congenital heart disease it is not known whether the defect is an intrinsic factor in the germ plasm or an extrinsic factor in the environment of the embryo It is rare to have a positive genealogic history of manifest congenital heart disease unassociated with another anomaly of the heart or the body

The occasional occurrence of rubella (German measles) in the first trimester of pregnancy is [illegible]
anomalies in [illegible]
cause in occa [illegible]

PATHOLOGY In many instances of congenital heart disease there is maldevelopment of different structures in the heart which are in close anatomic association. *In some* instances when there are abnormal changes in pressure in the chambers of the heart or

are a small and usually paradoxical pulse, low systolic blood pressure and especially a low *pulse pressure, and little* or no evidence of pulmonary congestion.

When the diagnosis is made, pericardiectomy is usually advisable.

Cardiac tamponade is manifested by a rising venous pressure, a falling arterial pressure, a small heart, tachycardia, a fall in blood pressure and clinical features of shock. This is a common form of heart failure in constrictive pericarditis

Systemic venous congestion is manifested by engorgement of the cervical veins, increased venous pressure, and enlargement of the liver. Cyanosis of the lips, face and neck and occasional facial edema is present

Paradoxical pulse, a distinct diminution in pulse amplitude during inspiration, may be associated with cardiac tamponade. It is best demonstrated by the fall in blood pressure of 10 to 20 or more, expressed in millimeters of mercury, at the end of inspiration A pulsus paradoxus is observed in any abnormal increase in pulmonary vascular capacity during inspiration, for instance, in laryngeal and tracheal obstruction.

Electrocardiographic abnormalities which seem to be distinctive are observed in more than one half of those who have pericarditis. There are changes in the ST segments and T waves and low voltage of all complexes. Similarities to the changes in myocardial infarction of the electrocardiograms may be confusing without the clinical history and physical and roentgenologic examinations

Paracentesis of the Pericardium. In tapping the pericardium by means of a trocar or aspirating needle care is exercised not to injure the pleura and the internal mammary arteries

The safest point is probably close to the left edge of the sternum in the sixth interspace. This interspace may not extend to the sternum, but even if the cartilages are in contact, a needle could probably be introduced at this point

The increased area in cases of distention from pericardial effusions has led to tapping in the fourth interspace, either at the left sternal margin or 1 inch (2 5 cm) from it, or at the fifth interspace 1½ inches (about 4 cm.) from the sternal margin, or by thrusting the needle upward and backward close to the costal margin in the left costoxiphoid angle

The Nature of Pericardial Fluids. *Hemopericardium* is commonly present in acute myocardial infarction due to coronary artery occlusion or follows rupture of the cardiac wall It may also be due to scurvy, leukemia or other hemorrhagic diseases The condition is usually manifested as a cardiac tamponade.

Hydropericardium is usually part of a generalized anasarca of congestive heart failure, glomerulonephritis and myxedema It may be part of a nutritional deficiency with hypoproteinemia. Hydropericardium may result from local causes which interfere with the venous return from the pericardial circulation, such as mediastinal tumors

Pneumopericardium results from traumatic perforation of the pericardium or perforation of a neighboring air-containing organ into the pericardium If there is a large quantity of air, there may be tympany on percussion of the precordium and metallic or clinking heart sounds on auscultation. If both fluid and air are present, loud, gurgling, splashing metallic sounds may be audible (bruit de moulin) There may also be a pericardial rub

Roentgenologic examination readily reveals the presence of air There may be a horizontal fluid level which moves with cardiac pulsations

PARASITIC DISEASES OF THE HEART

The heart and the heart muscle are susceptible to invasion by developmental forms of *Trichinella spiralis, Tinea solium, Echinococcus granulosus* and *Metagonimus yokogawai* and other less well known parasitic worms

The pathologic changes and symptoms are slight and the results of examination are essentially negative unless there is a systemic invasion by the ova, and then the symptoms are comparable to those present in the larval infection by the pork tapeworm.

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ETIOLOGY In congenital heart disease it is not known whether the defect is an intrinsic factor in the germ plasm or an extrinsic factor in the environment of the embryo It is rare to have a positive genealogic history of manifest congenital heart disease unassociated with another anomaly of the heart or the body

The occasional occurrence of rubella (German measles) in the first trimester of pregnancy is associated with a significant incidence of congenital cataracts and cardiac anomalies in the offspring. Fetal endomyocarditis and syphilitic myocarditis may be the cause in occasional cases (see Viral Diseases, Chapter 17)

PATHOLOGY In many instances of congenital heart disease there is maldevelopment of different structures in the heart which are in close anatomic association. In some instances when there are abnormal changes in pressure in the chambers of the heart or

great vessels, the fetal openings may not close. For instance, a patent foramen ovale or a patent ductus arteriosus may serve as a compensatory mechanism when there is atresia or stenosis of a valvular orifice

SYMPTOMS Congenital heart disease symptomatically has been classified by Abbott into three groups· cyanotic, acyanotic, and potentially cyanotic, the last being subdivided according to the intensity of the cyanosis if cyanosis develops

Cyanosis. Cyanosis is usually associated with severe multiple cardiac anomalies which lead to death before the patient reaches the age of active childhood

When cyanosis appears at birth or shortly thereafter the child is called a blue baby or is said to have morbus caeruleus. The term blue baby should be used cautiously because cyanosis at birth is often due to pulmonary atelectasis or intracranial hemorrhage. Cyanosis may be absent at birth and may make its appearance later when a compensating open ductus arteriosus becomes obliterated

The cyanosis appears in the lips, tips of fingers or toes, nose, ears and mucous membranes In an interruption of the aortic isthmus, cyanosis is limited to the lower extremities

A secondary polycythemia is often associated with an intense cyanosis Erythrocyte counts of between 6,000,000 and 7,000,000 per cubic millimeter with concentrations of hemoglobin correspondingly elevated (110 to 130 per cent) are observed in a patient who has moderate cyanosis and occasionally higher in extreme polycythemia. Cyanosis appears when there is an oxygen unsaturation of 6 5 volumes per cent in the capillary blood

On decrease of the cardiac reserve there is dyspnea on exertion. Dyspnea may come in paroxysms and may be associated with an intensification of cyanosis and the presence of polycythemia Dyspnea if due to pulmonary congestion is accompanied by cough.

Cerebral anoxia is manifested by faintness, dizziness and headache. Severe cerebral anoxia may cause syncope, convulsions, delirium, paralyses and coma

Peripheral vascular disturbances in the extremities include coldness, numbness and tingling or pain irrespective of the presence or absence of cyanosis and polycythemia.

The origin of clubbing of the fingers and perhaps the toes, whether in those who have congenital heart disease or other conditions, is difficult to correlate with the recorded findings concerning oxygen unsaturation, capillary stasis, an increased blood flow and maximal heat elimination from the fingers (see The Hand, Chapter 6)

Acyanosis. In the absence of cardiac failure some congenital cardiac patients *may never have cyanosis Those who do not have cyanosis* do not have a venous arterial anastomosis.

EXAMINATION On examination the presence of a cardiac murmur, enlargement of the heart, or dyspnea, with or without cyanosis and clubbing, without bronchopulmonary disease or brain injury, which commenced in infancy or early childhood is indicative of congenital heart disease

In early infancy the *cardiac murmurs* of congenital heart disease tend to be generalized but in time they will assume the site of predilection for their maximal intensity and thus reveal their identification A rough, loud murmur with maximal intensity in the second left interspace near the sternum may be due to a pulmonic stenosis, patent ductus arteriosus, or the tetralogy of Fallot The murmur of pulmonary stenosis is systolic and the second pulmonic sound is enfeebled. The murmur of a patent ductus arteriosus is a machinery-like murmur extending through *all* or a greater part of the cardiac cycle In aortic septal defect the machinery-like murmur is loudest over the lower part of the sternum or in the fourth left interspace

A loud systolic murmur, with maximal intensity in the third or fourth interspace to the left of the sternum, often transmitted to the left scapular region, is present in

interventricular septal defect (maladie de Roger). If there is an associated mitral stenosis, a later diastolic apical murmur may be audible. Systolic murmurs in the interscapular regions, in the axilla or along the sternum are present in instances of adult coarctation of the aorta when there is a well-developed collateral circulation.

A definite thrill in the second, third or fourth left interspace near the sternum in the absence of acute thoracic trauma is significant of congenital heart disease.

Roentgenologic examination of the thorax is invaluable in confirming suspected instances of dextrocardia, coarctation of the aorta, right-sided aortic arch and other abnormal cardiac silhouettes indicating lesions which might otherwise not be suspected.

Angiocardiograms and *arteriograms* may give objective demonstration of coarctation of the aorta, patent ductus arteriosus, aortic arch anomalies and aneurysm. In cases of coarctation not only is the diagnosis made but the site and type, which are of greatest value in preoperative planning, are delineated Retrograde visualization is decisive in borderline instances of patent ductus arteriosus. The simultaneous opacification of aorta and pulmonary artery or the actual demonstration of the ductus is objective evidence of patency. Aortic arch anomalies can be outlined. In aneurysms that are filled with clot, often there is enough evidence in the aortogram to make the diagnosis. Angiocardiography is not a method without some potential hazard

In *studies of circulation time* the presence of a venous-arterial communication may be demonstrated by the administration of drugs (ether and saccharin) as in the tests for determining the circulation time. Such tests are particularly useful in instances of the tetralogy of Fallot and terminally in cases of auricular or ventricular septal defects or patent ductus arteriosus when the usual left-to-right communication has been reversed. These tests are useful in trilocular or bilocular hearts or in those patients in whom there are extensive septal defects.

Intracardiac catheterization is a test to be employed only by skilled hands and even then it is not without danger

COMPLICATIONS The complications of congenital heart disease are congestive heart failure, bacterial endocarditis, cerebral abscess or hemorrhage, and paradoxical embolism Pulmonary tuberculosis often is a serious complication of congenital heart disease

The term paradoxical embolism refers to the passage of a thrombus from systemic veins to the arterial circulation, usually through a patent foramen ovale. A diagnosis of paradoxical embolism during life cannot be made

SOME CLINICAL TYPES OF CONGENITAL HEART DISEASE

Atrial Septal Defects. The clinical syndrome associated with atrial septal defects occurs most often when the septal defect is combined with mitral stenosis

Symptoms may be absent Often a normal span of life is enjoyed If symptoms are present owing to an atrial septal defect, they frequently arise from an associated paroxysmal tachycardia and transient auricular fibrillation Once symptoms become manifest, they often terminate in congestive heart failure

On *physical examination* there may be a left-sided deformity of the thorax. Palpation and percussion reveal enlargement of the heart, the apex being displaced downward and to the left while the right border is extended to the right of the sternum

A loud systolic murmur, sometimes accompanied by a thrill, is heard in the second or third interspace near the left border of the sternum or at the apex In about one third of these patients there is an apical diastolic murmur of mitral stenosis. The second pulmonic sound often is accentuated

Electrocardiographic examination may reveal a right axis deviation or auricular fibrillation or right bundle-branch block.

The results of *surgical treatment* by attempts to close septal defects are encouraging

Ventricular Septal Defects (Roger's Disease). Ventricular septal defects are

often associated with dextroposition of the aorta and pulmonic stenosis as well as other defects. There are usually no symptoms due to the lesion itself. Sometimes cyanosis is present at birth but disappears.

On examination there is a prolonged, loud and harsh systolic murmur with maximal intensity in the third or fourth left interspace near the sternum. Rarely the murmur is loudest at the left of the xiphoid process Often it is transmitted to the back where it is heard in the left interscapular or subscapular region. The murmur may obscure the second sound. In about one third of the cases the murmur is accompanied by a systolic thrill.

The Tetralogy of Fallot. The combination of a ventricular septal defect with pulmonary stenosis, dextroposition of the aorta and right ventricular hypertrophy is known as the tetralogy of Fallot.

The lesions in the tetralogy of Fallot are attributable to two essential factors of maldevelopment: (1) an adequate clockwise torsion or even a counterclockwise torsion of the truncus and bulbus arteriosus and of the septum which divides this vascular tube and (2) persistence of the (reptilian) right aorta which normally atrophies

SYMPTOMS Cyanosis is present at birth or it may have appeared after several months of age when the ductus arteriosus closes The cyanosis may become intensified during exercise, pulmonary infections and late in the course of the disease when heart failure develops Suffusion of the eyeballs is often associated with secondary polycythemia

Dyspnea on exertion is common Paroxysmal attacks of dyspnea may occur, generally after exercise and accompanied by an intensification of cyanosis. The dyspnea may be intensified when the patient is erect (orthostatic dyspnea) Characteristically the patient who has tetralogy of Fallot assumes the squatting or knee-chest posture when dyspneic or freshly tired.

EXAMINATION. Precordial bulging, systolic pulsation in the second and third interspaces, and epigastric pulsation may be present and if so they are due to the hypertrophy of the right ventricle Usually there are a systolic murmur and thrill to the left of the sternum in the second or third interspace, occasionally in the fourth. The second pulmonic sound is normal, weak or absent

Clubbed fingers are usually present when cyanosis is of long duration In some instances clubbed fingers may be present without cyanosis (see The Hand, Chapter 6).

Patent Ductus Arteriosus. Anatomic closure of the ductus is normally accomplished by the end of the third postnatal month in 4 of every 5 who have this anomaly

In uncomplicated patency of the ductus arteriosus the higher pressure in the aorta permits blood from that vessel to pass into the pulmonary artery during both systole and diastole There may be a reversal of the flow during crying, sucking, coughing, pulmonary infections and in the presence of heart failure

SYMPTOMS When symptoms appear, they are most often dyspnea on exertion and palpitation

EXAMINATION. Those who have patent ductus are pale, slender, undernourished and poorly developed. The left ventricle is enlarged There is a long and rumbling murmur which may extend through the heart cycle The murmur may be diffuse but usually is localized or loudest in the second left interspace near the sternum The murmur may not be continuous, it may be a long systolic murmur with maximal intensity in the second left interspace, near the sternum In other instances only a diastolic murmur may be heard to the left of the sternum The second pulmonic sound is accentuated and may be reduplicated. There often is a continuous thrill over the precordium.

When the ductus arteriosus is widely patent, there is a high pulse pressure, and signs remindful of aortic regurgitation are present.

When surgical treatment is contemplated, the cardiologist must recognize whether the patent ductus arteriosus is or is not associated with cardiac anomalies In some cardiac anomalies patency of the ductus is essential to the maintenance of life, and therefore it is well to recognize such cases before attempting surgical intervention Some of these anomalies are. infantile coarctation of the aorta, transposition of the great vessels and pulmonary atresia and stenosis.

Persistent Truncus Arteriosus Communis. As the result of defective development of the bulbar septum there may be a common arterial trunk instead of distinct aorta and pulmonary artery.

If the pulmonary arteries arise directly from the truncus arteriosus, cyanosis is absent or minimal More often the circulation through the lungs is by way of dilated bronchial arteries; in such cases cyanosis is usually intense.

A harsh systolic murmur and thrill and cardiac enlargement are present. Roentgenologic examination discloses characteristic findings which are recognizable by the roentgenologist.

DISEASES OF THE THORACIC ARTERIES

DISEASES OF THE PULMONARY ARTERIES

Pulmonary Arteriolar Sclerosis. The existence of primary pulmonary arteriolar sclerosis cannot be proved during life

In secondary pulmonary arteriolar sclerosis, such as is present in chronic pulmonary emphysema, the small pulmonary arteries and arterioles may be the site of arteriosclerosis. The pulmonary arteriosclerotic lesions are probably secondary to pulmonary hypertension and not the cause. As a rule, the right ventricular enlargement in emphysema is due to secondary changes in the pulmonary capillary system which are unlikely to cause significant obstruction.

The manifestations of pulmonary arteriolar sclerosis are those of chronic cor pulmonale

Ayerza's Disease or Syndrome. The terms Ayerza's disease and Ayerza's syndrome refer to a clinical syndrome associated with bronchopulmonary symptoms and characterized by intense cyanosis, polycythemia and congestive heart failure. Formerly this disease was thought to be a syphilitic process

Pulmonary Arteriovenous Aneurysm. There are often cutaneous, mucosal and visceral angiomas, frequent occurrence of telangiectasia or recurrent epistaxis in parents or siblings (hereditary hemorrhagic telangiectasia).

The essential manifestations of pulmonary arteriovenous aneurysm are cyanosis and clubbing of the digits, in the presence of a normal heart, together with roentgenographic findings of a vascular tumefaction in the lung. Bleeding from the nose is common Hemoptysis may be lethal There may be headache, vertigo, weakness, syncope, convulsions, paresis or paresthesia of the extremities, dysphagia and hoarseness

There is an increase in the erythrocyte count and in the hemoglobin content. The total blood volume in the polycythemic cases is increased, but the plasma volume shows little or no increase in contradistinction to the observation in peripheral arteriovenous fistula The peripheral arterial oxygen saturation is decreased.

THE AORTA

The *ascending aorta* begins behind the left half of the sternum on a level with the lower border of the third costal cartilage It proceeds upward, forward and toward the right until it reaches the level of the lower border of the right second costal cartilage, where the horizontal portion of the arch begins

Immediately above its commencement it has three enlargements, two anteriorly and one posteriorly, called the sinuses of the aorta (Valsalva), which correspond to the semilunar valves From the sides of the posterior enlargement the right and left coronary arteries arise

Distal to the valves in the upper right portion of the arch, the aorta is again dilated, forming the great sinus of the arch of the aorta

The right limit of the aorta is about even with the right edge of the sternum; sometimes it projects slightly beyond. Because of the proximity of the aorta to the second interspace, it is here that the stethoscope is placed to hear aortic murmurs. The aorta at this point is covered only by the thin border of the right lung and pleura and the slight remains of the thymus

The first portion of the aorta is not united with the pericardium, but simply loosely covered by it, so that this portion of the arch is weaker than the other portions, and rupture, with extravasation of blood into the pericardial sac, is not uncommon

The *horizontal* or *transverse* and *descending* portions of the *aorta* pass anteroposteriorly from the upper border of the second right costal cartilage in front to the left side of the body of the fourth thoracic vertebra or its intervertebral disk posteriorly. This part of the aorta is about 2 inches (5 cm.) long Its undersurface is level with the angle of the sternum (angle of Ludwig), opposite the second costal cartilage Its upper surface rises as high as the middle of the first piece of the sternum, which is opposite the middle of the first costal cartilage, about 1 inch (2.5 cm.) below the top of the sternum. It describes a double curve in its course, with one concavity downward corresponding to the root of the left lung and another to the right corresponding to the trachea.

The *ductus arteriosus* at birth is about ⅖ inch (1 cm.) long and runs from the pulmonary artery near its bifurcation or from the left pulmonary artery to the undersurface of the arch of the aorta a little beyond the point where the left subclavian artery arises from its upper convex surface It serves in the fetus to carry the blood from the trunk of the pulmonary artery direct to the aorta instead of passing into the lungs When, after birth, the lungs are used, the ductus arteriosus becomes obliterated and is found later in life as a cord running to the underside of the arch of the aorta

Aortic Septal Defect (Aneurysm of Sinus of Valsalva). Aortic septal defects consist of (1) a small opening between the aorta and pulmonary artery just above the semilunar valves, and (2) thinness of the septum between the vessels As the result of the thin septum an aneurysm forms of the right sinus of Valsalva or, more rarely, of the posterior sinus. These aneurysms are clinically significant because of a tendency to perforation. In either case the symptoms and signs resemble those of patency of the ductus

The diagnosis is suggested by the sudden occurrence, without apparent cause, of symptoms of progressive heart failure and signs of a communication between the aorta and right side of the heart, a continuous or harsh systolic murmur and thrill.

Death may occur suddenly

Coarctation of the Aorta. There are two forms of coarctation of the aorta, the infantile and the adult The infantile form is characterized by diffuse involvement of the aortic isthmus. Also, this anomaly may be associated with other congenital anomalies, including a patent ductus The adult form is a more localized constriction at or below the insertion of the ductus and usually occurs in boys and men

The heart has a hypertrophied left ventricle. The adult form of coarctation often is associated with a bicuspid aortic valve Congenital subaortic stenosis and aortic insufficiency occur occasionally in cases of adult coarctation, with or without bicuspid valves Miliary aneurysms of the small cerebral vessels are frequent in the region of the circle of Willis

Symptoms are often absent except for those referable to the hypertension in adults The first symptom in a young adult may be sudden hemiplegia.

The objective findings on examination consist of bilateral supraclavicular pulsations in dilated tortuous collateral vessels and in the large subclavian arteries. The collateral vessels are often most noticeable along the inner borders of the scapula and across the scapular area, in the axilla or less often along the sternum or in the epigastrium

The heart is enlarged to the left and downward. There is a moderately loud systolic murmur over the precordium, most intense at the base, but often heard also in the left interscapular region The murmur, sometimes louder in the back than anteriorly, is accompanied by a thrill. There may also be murmurs of aortic stenosis and insufficiency.

There is no palpable aortic pulsation in the abdomen The femoral pulses are weak or impalpable. [illegible] d demonstrable unless

In the a [illegible] extremities, the blood there is hear [illegible] Normally the systolic pressure in [illegible]

blood pressure in the femoral artery is about 20 mm. higher than in the brachial artery. In cases of adult coarctation the brachial systolic pressure is considerably higher than the femoral systolic pressure.

The roentgenologic finding of erosions of the lower borders of the ribs by the large collateral vessels is diagnostic. The erosions may involve a variable number of ribs from the third to the tenth, usually on both sides and in their posterior portion. The erosions are localized and smooth

Preoperative demonstration of the site of the stenosis and its relation to the left subclavian artery is of value to the surgeon. Employment of intravenous cardiography with the aid of diodrast is often effective in revealing the site of occlusion or stenosis of the aorta and often its approximate length and caliber can be estimated In addition angiocardiographic examination may disclose the presence of associated congenital valvular lesions and the state of the collateral circulation, particularly the size of the internal mammary arteries and the aortic branches proximal to the coarctation

The diagnosis of coarctation of the aorta depends on the presence of hypertension, with weak or absent femoral pulse and with blood pressure less in the lower than in the upper extremities. Confirmatory diagnostic data are palpable collateral vessels, a systolic murmur which is as loud in the interscapular region as it is over the precordium, or louder, and roentgenologic observation of erosion of the ribs or defect in the aortic arch

About 1 of every 4 adults who have coarctation attains a relatively normal life span and dies of incidental causes Some may have this disease and it is never known

The commonest complications and causes of death are congestive heart failure, bacterial endocarditis or aortitis, rupture of the aorta and cerebral hemorrhage.

Surgical Treatment. Experience to date suggests that the optimal time for surgical treatment, if this is considered, is between the ages of 6 years and 20 years. In patients more than 20 years of age in many instances the aorta exhibits regional atherosclerosis of sufficient degree to impair the ease and safety of surgical manipulation

Right-Sided or Double Aortic Arch. A persistent right aortic arch or double aortic arch is clinically insignificant It attains clinical importance if physical disturbances arise from its presence

If symptoms appear, they consist of dysphagia and dyspnea by compression of the esophagus or trachea In those in whom the descending aorta crosses to the left, compressing the left recurrent laryngeal nerve, attacks of croup and brassy cough may result When there is a double aortic arch together with an aberrant left subclavian or patent ductus or ligamentum arteriosum forming a vascular ring around the trachea and esophagus, noisy, stridulous breathing, mild dysphagia and chronic cough may occur.

The right-sided aortic arch attains clinical importance when it is to be differentiated from a mediastinal tumor, lymphoma or aneurysm.

The diagnosis is made by roentgenologic examination

Syphilis of the Aorta. *Treponema pallidum* enters the blood stream early in the infection and localizes in the ascending aorta

Between 15 and 25 years often elapse between the onset of the primary syphilitic infection and the appearance of clinical manifestations of cardiovascular disease. The clinical symptoms and signs appear only when the aortic lesions are sufficiently severe and extensive or involve the coronary ostia and aortic valves

Manifested aortic syphilis is most frequent between the ages of 35 and 55 years. The acquired disease, however, has been recorded as late as the age of 70 years and as early as 20 years. Cardiovascular syphilis affects men predominantly. There is a higher incidence of aortic syphilis in Negroes than in whites. There is no

evidence that this is necessarily due to racial susceptibility It is due to the incidence of the disease in this race.

Despite the frequency of congenital syphilis it rarely produces cardio-aortic lesions of the type seen in acquired syphilis.

The gross appearance of syphilitic aortitis is characteristic The distinctive features are the bluish gray plaques without atheroma; the wrinkling and puckering of the intima with a tendency to form parallel grooves in the direction of the long axis of the vessel, and the demarcation of the lesions ending at or before the origins of the vessels of the neck, at the level of the diaphragm or at the origin of the renal arteries. The aorta loses its elasticity and becomes widened and flaccid.

Aortic insufficiency is the result of a widening of the lumen of the vessel and not of direct valvular involvement. There is a destructive inflammation of the aortic wall resulting in dislodgment of the cusp attachments at the commissures

The syphilitic etiology of the valvular lesion is indicated by evidence of syphilis absence of a history of rheumatic fever in childhood, absence of mitral stenosis, *and by the presence of a systolic and diastolic murmur, loudest in the second right* interspace The association of both syphilitic and rheumatic valvular disease may occur

Syphilitic aortic insufficiency is often well compensated for a long time, during which the only symptoms present are palpitation, pounding in the ears or uncomfortable pulsations in the head and neck.

There are frequently no symptoms referable to syphilitic coronary ostial stenosis unless severe involvement is present The diagnosis of syphilitic coronary ostial stenosis is considered when there are syphilitic aortitis and aortic insufficiency, if the patient has angina pectoris. In the absence of evidence for syphilis, angina pectoris is almost always due to coronary arteriosclerosis

On examination there is present a tambour-like second aortic sound, which is not characteristic of syphilis A similar second sound is frequently heard in the presence of aortic atherosclerosis

[illegible] may be considered when there is roentgeno- [illegible] a patient who is less than 40 years old, [illegible] ave hypertension or rheumatic valvular disease In patients aged more than 40 years, who present all the characteristic findings, the diagnosis may be either an aortic arteriosclerosis or a syphilitic aortitis.

Calcification of the Aorta. Calcification of the aorta occurs as a part of a generalized atherosclerosis in middle-aged and aging persons If any clinical manifestation is present it consists of a rough, harsh, basal aortic murmur The murmur arises from interference with the flow of blood into or in the aorta by atheromatous plaques situated in or just distal to the aortic valves.

The calcification is revealed by roentgenologic examination However, many aortas contain calcifications without causing clinical manifestations

Aortic Aneurysm. Aortic aneurysm results from an extensive syphilitic aortitis or atherosclerosis The aneurysms of syphilitic aortitis occur in younger patients (40 to 50 years) while those of atherosclerosis occur in older patients In either case the blood pressure in the vessels serves to dilate the vessel slowly; as a result localized dilatation or sacculation occurs and thus an aneurysm ensues.

Aneurysm of the aorta may remain asymptomatic until rupture and death If symptoms occur, they are those of mediastinal pressure (see Chapter 9). Sudden death is common

The ascending aorta is most frequently involved and is most likely to be associated with both angina pectoris and congestive heart failure. Aneurysm of the ascending aorta, termed *aneurysm of physical signs*, is commonly saccular in type As it enlarges, it extends upward, compressing the right bronchus and lung and the superior vena cava and presenting on the surface of the thorax at the second or

third ribs to the right of the sternum It may also compress the pulmonary artery. A few physicians have seen these visible tumors oozing blood through the skin just prior to their rupture.

Aneurysm of the arch, termed *aneurysm of symptoms*, may compress the esophagus, the left bronchus, the left recurrent laryngeal nerve and the sympathetic nerves and is thus prone to produce symptoms early.

In all of these aneurysms thoracic pain and cough are the commonest complaints. The pain is persistent and may be severe. The dry cough may have a brassy quality and there may be hoarseness (paralysis of the recurrent laryngeal nerve). Soon the cough is associated with expectoration, and more rarely with hemoptysis, both due successively to bronchostenosis, atelectasis and bronchiectasis. Atelectasis, bronchopneumonia, abscess or bronchiectasis may arise not only from tracheal or bronchial compression but also from direct invasion of the lung by the aneurysm. Owing to pressure on the trachea or on a bronchus, inspiratory stridor may develop

On examination by physical means the findings are those of a mediastinal tumor. The heart is not enlarged as a result of aneurysm itself. Inspection and palpation may reveal a pulsation in the anterior thoracic wall in the second or third right interspace, or higher, or to the left. There may be inequality of the pupils and unilateral exophthalmos. Suffusion of the face, neck and upper extremities with cyanosis and edema may be present as the result of pressure on the great veins

A systolic thrill, a diastolic shock, and a tracheal tug downward, synchronous with the heart beat, may be felt The right radial pulse may be diminished in amplitude, delayed or obliterated by partial obstruction of the orifice of the innominate artery A decrease in blood pressure is constant in the arm in which the pulse is decreased

Systolic murmurs are often present over the aneurysm Diastolic murmurs are due to associated aortic insufficiency.

Aneurysm of the *descending aorta* may reach a large size before it produces symptoms When symptoms are present, there are thoracic pain, dyspnea and cough Dysphagia is an occasional symptom resulting from pressure on the esophagus. There is a visible pulsation on the posterior thoracic wall either below and to the left of the left scapula or somewhat higher in the interscapular region.

Syphilitic aneurysm of the *abdominal aorta* occurs in those less than 50 years of age Arteriosclerotic abdominal aneurysm occurs any time from the age of 40 years on The syphilitic aneurysm usually occurs at the level of the celiac axis

The commonest symptom of abdominal aneurysm is pain in the abdomen or back It may be paroxysmal, or constant and boring. There may be root pains extending from the back to the upper part of the abdomen These and other symptoms result from erosion of the vertebrae, or pressure on the spinal cord, gastrointestinal tract, ureter or other abdominal structures. Death is usually caused by rupture of the sac into the peritoneal cavity, gastrointestinal tract or retroperitoneal space Most abdominal aortic aneurysms are asymptomatic.

Examination may reveal an expansile pulsating mass, palpable thrill, and audible bruit, and occasionally a difference in the femoral pulsations. Roentgenologic examination may disclose an abdominal mass with or without calcification and erosion of the anterior vertebral bodies from the eleventh thoracic to the second lumbar

Diagnosis of aneurysm is made by evaluation of the history, physical and roentgenologic findings Roentgenograms of the thorax, and angiocardiograms, if necessary, usually provide the necessary diagnostic data to distinguish aneurysms from other conditions. When aortic aneurysm is suspected, bronchoscopic and esophagoscopic examinations are contraindicated because of the danger of hemorrhage.

The prognosis in syphilitic aortitis is better than in aortic insufficiency, aneurysm or coronary stenosis.

Dissecting Aneurysm of the Aorta. The etiology of this condition is a matter of conjecture. Among the more commonly accepted causes are (1) degenerative changes in the wall of the aorta, (2) congenital defects, (3) mechanical causes, (4) inflammatory reactions and (5) trauma.

The initial symptoms of a dissecting aneurysm of the aorta may be pain and unconsciousness, pain and convulsions, hemiplegia, and vertigo. The symptoms commence as an acute violent pain in the thorax, back or abdomen with a feeling of impending death or annihilation. The pain tends to migrate in steplike fashion from one region of the body to another, suggesting the course of progression of the dissection In contrast to the pain of coronary disease the pain of dissecting aneurysm is not frequently experienced in the arms, but pain and paresthesia are common in the lower limbs. In some instances the pain may never be severe even with rupture.

The neurologic symptoms associated with dissecting aneurysm of the aorta are exceedingly variable and when present result from ischemic necrosis of the brain, spinal cord or peripheral nerves It is difficult to be certain whether the presenting symptoms are of cerebral, spinal or peripheral nerve origin.

The findings on examination depend on the situation of the dissection and the organs affected. Prior to rupture there are no localizing signs After rupture examination is not necessary. Prior to rupture the blood pressure is maintained. The temperature remains normal The leukocyte count is usually elevated.

Examination of the heart may give but little helpful information The presence of a cardiac murmur and the appearance of a precordial rub during the course of the illness are of diagnostic importance The electrocardiogram may show evidence of ventricular strain or other changes, which, however, are not of a specific pattern common to dissecting aneurysm of the aorta. Roentgenologic examination of the chest may reveal helpful information and may even establish the diagnosis. Occlusion of an artery to one of the extremities may be found.

DIAGNOSIS. *The diagnosis of dissecting aneurysm* depends on the sudden onset of severe and usually prolonged and migrating pains and roentgenographic findings of enlarged heart with tortuous aorta which may be dilated and calcified

[illegible] disease cerebral vascular con- [illegible] affections of the spinal cord such as abscess, hemorrhage or myelitis, and [illegible] acute arterial occlusive conditions. Occasionally the symptoms are such that abdominal exploration is carried out and this procedure may not be diagnostic.

Death in the majority of patients is due to an external rupture into one of the body cavities

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Examination of the heart may give but little helpful information The presence of a cardiac murmur and the appearance of a precordial rub during the course of the illness are of diagnostic importance. The electrocardiogram may show evidence of ventricular strain or other changes, which, however, are not of a specific pattern common to dissecting aneurysm of the aorta. Roentgenologic examination of the chest may reveal helpful information and may even establish the diagnosis Occlusion of an artery to one of the extremities may be found.

DIAGNOSIS. The diagnosis of dissecting aneurysm depends on the sudden onset of severe and usually prolonged and migrating pains and roentgenographic findings of enlarged heart with tortuous aorta which may be dilated and calcified.

The differential diagnosis includes acute cardiac disease, cerebral vascular conditions, abdominal diseases, thoracic or pulmonary diseases, affections of the spinal cord such as abscess, hemorrhage or myelitis, and finally acute arterial occlusive conditions Occasionally the symptoms are such that abdominal exploration is carried out and this procedure may not be diagnostic.

Death in the majority of patients is due to an external rupture into one of the body cavities

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11

DISEASES OF THE URINARY ORGANS

Diseases of the urinary organs comprise the disorders of the kidneys, ureters and bladder The diseases of the male urethra, which combines the functions of a genital and a urinary organ, are discussed with the diseases and conditions of the external genitalia of the male (Chapter 7).

DISEASES OF THE KIDNEYS

Examination of the Kidneys The kidneys extend from the level of the twelfth thoracic vertebra to the third lumbar vertebra. The twelfth rib passes across each kidney at about its middle.

The position of the right kidney is a little lower than that of the left The right kidney is in contact above with the liver; the left kidney lies adjacent to the spleen. At the medial concave margin of each kidney are the renal vessels as well as the renal pelvis and the renal calyces (major and minor).

Palpation. An imaginary perpendicular line extended from the midclavicular line, at a point 2 fingerbreadths below the costal arch, into the depth of the abdomen will reach the normal kidney, for this organ normally extends for a distance of 2 to 2⅖ inches (about 5 to 6 cm) below the costal margin in the midclavicular line.

On attempting to palpate the kidneys, *bimanual palpation* is employed Thus, on palpating the right kidney, the right hand is placed flat on the abdominal wall in front and, during expiration, presses into the depth. The fingers of the palpating hand are directed upward, the tip of the middle finger reaching a point 2 fingerbreadths below the costal margin on the clavicular line. The fingers of the left hand press the kidney forward from behind while the thumb of this hand holds the liver up (Fig 11-1).

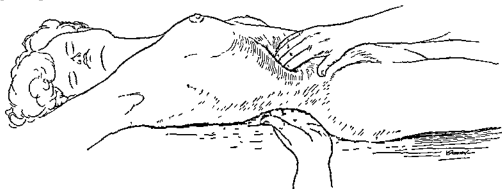


Fig 11-1 Bimanual palpation of kidney.

In addition to the dorsal recumbent position, the lateral, the ventral, the sitting and, especially, the upright postures are employed if needed to delineate the kidney, assuming, of course, that the patient is physically able to take these positions

Perhaps one of the best methods for palpating a kidney is to desire the patient to lie on the back, knees flexed The patient then passes the forearm, *on the side* to be examined, across the back at a right angle to the spinal column with the palm

of the hand downward, and thus lies on the arm and hand, and breathes deeply while the examiner palpates for the kidney.

The normal kidney is not always palpable The palpability of its lower extremity depends on the amount of obesity of the abdominal wall and of the intestine as well as on the degree of distention and on the skill of the examiner. If more than the lower third or the lower half of the kidney is palpable on deep inspiration, the condition is abnormal. When palpable, the surface of the normal kidney is felt as a smooth surface with bluntly rounded margin

The ptosed kidney can be recognized by its absence from its normal position and by the fact that it can be shoved back into its normal position (palpable kidney, floating kidney, wandering kidney). It is 10 times as frequent in women as in men and is usually associated with ptosis of other organs The left kidney is oftener congenitally dystopic than the right The excursion of a ptosed kidney is well demonstrated by employment of intravenous urography

Besides being palpable when displaced, the kidney may become palpable when renal enlargement exists owing to tumors, cysts, hydronephrosis, abscess or tuberculosis. If the kidney is tender, the tenderness often results from renal tuberculosis, pyelonephritis or renal abscess

A kidney may be definitely enlarged and yet not palpable, especially in renal calculus and in renal tuberculosis Obesity or abdominal distention from any cause may interfere with palpation

In deciding whether a kidney is enlarged or whether the structure palpated is an enlarged liver, gallbladder, pancreas, or spleen, the exact topographic situation of the structure is delineated and its relation to the gastrointestinal tract and its mobility are observed. The final decision will have to rest on the findings revealed by the intravenous urogram, ureteral catheterization and functional renal diagnosis. Any pain which may occur in the region of a kidney may be diagnostically perplexing, and for this reason roentgenologic examination of the spinal column is often necessary.

Renal tumors lie rather lower and further to the side of the abdomen than most other tumors, later growing forward toward the anterior abdominal wall so as to fill up the hypochondrium and perhaps displace the liver and diaphragm. Renal tumors lie *behind the colon*

Roentgenology in Urologic Examination The objective means of diagnosis of renal calculus (nephrolithiasis) and of dilatation or contraction of the renal pelves is the intravenous urogram, often supplemented by ureteral catheterization and injection of opaque media Inability of a kidney to concentrate the material used for intravenous urography is a rough and often an inaccurate determination of renal functional activity.

THE EXCRETORY CAPACITY OF THE KIDNEYS The *composition of normal urine,* 24-hour volume, 1,000 to 1,800 ml, specific gravity 1 015 to 1.025, varies insignificantly from day to day. Wide variations in composition may be observed in urine of successive urinations during a single day Urinalysis is made on a well-mixed 24-hour specimen All the urine voided during 24 hours is collected in a clean vessel containing a few drops of a preservative (toluene) and stored in a cool place The bladder is emptied and the urine is discarded before beginning the collection period, the final collection should be made at the end of the 24-hour period

Routine examination of the urine includes macroscopic inspection, determinations of specific gravity and acidity or alkalinity, tests for albumin, sugar, bile, acetone and diacetic acid, and a microscopic examination for cellular elements and bacteria. When bacteriologic study is desired, the specimen is collected by catheterization with the aid of aseptic apparatus and technic.

Physicians have long known the importance of recording the intake of water and

the quantity of urine excreted as a guide in judging the renal functions. The *oliguria* in many cases of acute nephritis, of chronic renal disease associated with dropsy, and of chronic passive congestion of the kidneys has been recognized. So also the *polyuria* resulting from the hard-working remnants of the kidney unable to concentrate urine—fixed specific gravity urine. The comparison of the quantity and the specific gravity of the *night urine* and of the *day urine* is a useful procedure, and one resorted to by many practical diagnosticians.

There are four determinations that should always be made when there is reason to suspect renal disease. (1) determinations of urinary concentrating power (the specific gravity), (2) estimation of proteinuria (albumin), (3) examination of the urinary sediment and (4) analysis of blood for nonprotein nitrogen (blood urea nitrogen). The serum creatinine should be determined if the urea is elevated. If nitrogen retention is present and there is reason to suspect acidosis, a determination of acid-base balance by means of carbon dioxide content or combining power and chloride level is made.

Abnormalities of Excretion of Urine. Oliguria and Polyuria. In *oliguria* the quantity of urine is markedly diminished. When oliguria is associated with albuminuria and cylindruria, especially if hematuria is present, there is organic renal disease, likely glomerulonephritis. In chronic passive renal congestion, oliguria is present with albumin and casts in the urine. These signs clear up when the circulation is restored and the renal stasis is overcome. Oliguria with essentially normal urine occurs in dehydration.

Polyuria (frequency of urination), when persistent, and when associated with urine of low specific gravity, often indicates a chronically diseased kidney and, on rare occasions, diabetes mellitus, or more rarely still, diabetes insipidus. Polyuria may occur in renal amyloid disease and in pyelitis. If the polyuria is associated with high specific gravity of the urine, diabetes mellitus is suspected since this association is rare in renal disease. The common cause of polyuria is nerve tension

Nocturia. Frequent urination during the night is common in renal disease and in prostatism In the latter disorder this is often the first sign noticed by the patient When this symptom is complained of, tests of functional capacity of the kidneys should be undertaken and the prostate examined

Abnormalities in the Excretion of the Constituents of the Urine. *Hyposthenuria.* In hyposthenuria the specific gravity is low, no matter what quantity of urine is passed It would appear that, in many of these conditions, the kidney is unable to secrete a urine of greater concentration

Hypazoturia. In some cases of renal disease the kidney is unable to eliminate nitrogenous substances adequately. This condition is often met with in association with high blood pressure without uremic symptoms and without edema. The nonprotein nitrogen of the blood is increased in amount Sodium chloride and water may be excreted fairly well in the urine.

Hypochloruria. Hypochloruria may be associated with edema Often the nitrogenous substances may be well eliminated, while sodium chloride is retained. In such cases addition of sodium chloride to the food leads t
an accentuation of the oliguria and an increase in the
chloride is retained, water accumulates in the tissues
In other cases relatively more sodium chloride may be retained than corresponds to physiologic salt solution, the edema in such cases may be slight, so that it is recognizable only by a slight increase in the body weight. In retention of water and salt extrarenal factors, such as cardiac decompensation and starvation, may be responsible.

The Low Salt Syndrome. The term low salt syndrome has been suggested by Schroeder. This syndrome or similar conditions have been observed and described previously, but the term low salt syndrome seems appropriate in order to unify data.

The syndrome appears to be a state of renal insufficiency dependent on a dis-

turbance of the normal concentration of sodium chloride in extracellular fluids. It is not dehydration, because large stores of fluids may be present It is not dependent on alkalosis, for the carbon dioxide-combining power of the blood may be altered only slightly. It can be initiated by depleting the body of sodium chloride through the use of either mercurial diuretics or other measures, by producing a large discrepancy between the intake and the output of fluid, or by excessive loss of salt through abnormal routes. It is often reversible by restoring the concentration of sodium chloride in body fluids to normal, a procedure which can cause diuresis and a return of renal function to higher values. It may accompany, but is not always dependent on, circulatory insufficiency; it is usually associated with prior renal disturbance, either functional or organic

It is probable that the excessive postoperative use of dextrose solution in water without sodium chloride contributes to renal insufficiency and initiates the low salt syndrome in elderly patients or in those who already have some renal disturbance of minor degree

SYMPTOMS The first symptoms observed by the patient or the members of the family or nurses are drowsiness, weakness and lethargy. There are a loss of appetite, nausea and occasionally vomiting In rare instances, particularly in prostatism with mild renal insufficiency, there may be symptoms of intestinal obstruction. The normally occurring muscular cramps in the low salt syndrome involve the muscles of the anterior abdominal wall as well as those of the back and legs and elsewhere. If the attention is directed to the abdominal distention and the cramps of the abdominal muscles to the exclusion of the other cramping muscles, too much emphasis may be placed on the abdominal symptoms which simulate intestinal obstruction

A history of a successive depression of urinary volume beginning from a few days to a week prior to the onset of symptoms is most helpful diagnostically. If the patient is one who knows his usual body weight, it will be evident that a gain in weight has occurred since the suppression of urinary output

EXAMINATION The physical findings vary and depend on the original illness, whether cardiac, postoperative, or renal disease, or prostatism There is a depression of urinary chlorides to negligible quantities which will not increase after injection of mercurial diuretics The concentrations of chloride and sodium in the plasma are low. An elevation of the concentration of nonprotein nitrogen in the blood is constantly present.

DIAGNOSIS. The diagnosis depends on awareness of the possibility of the condition and the finding of little or no chloride in the urine with a greatly decreased level of chloride in the plasma.

The Excretion of Abnormal Substances in the Urine. The list of substances which may appear in the urine which are present or found in traces in the normal urine is an extensive one Enumeration of these substances will not be made here since they are given in other parts of this text Reference should be made to discussions of diseases of metabolism (Chapter 22) and of poisoning by organic and inorganic chemicals (Chapter 19)

It is appropriate here to mention orthostatic albuminuria, cylindruria, hematuria, pyuria and bacteriuria, idiopathic hematuria and nonparasitic chyluria

Orthostatic Albuminuria. This albuminuria appears as the true or idiopathic form, as an albuminuria with an orthostatic response, and in association with latent and chronic glomerulonephritis

In the *true or idiopathic orthostatic albuminuria*, albumin occurs in the urine when the patient is in the erect position A specimen of urine excreted while the patient is in the lying position is free of albumin Some of these patients, however, may excrete a small amount of albumin immediately after lying down

Albuminuria with an orthostatic response is characterized by the presence of

albumin with the patient in any position, but in greater amounts while in the upright position.

In *chronic latent glomerulonephritis* there is a history of acute nephritis which has subsided and of albuminuria which has persisted. This condition differs from the usual orthostatic albuminuria by the excretion of traces of albumin during the night or when in the reclining position.

In all who have albuminuria, renal disease of some sort is present The nature of the renal abnormality in idiopathic orthostatic or true orthostatic albuminuria is not known. A patient who has a true orthostatic albuminuria is no more likely to have renal disease than a normal person In all the rest of those who have an orthostatic element in the excretion of albumin in the urine, there will be usually a normal response to all of the tests of renal functional activity.

There are no symptoms The albuminuria is discovered when the patient takes a routine physical examination, such as an examination for life insurance or for military service or entrance to a military institution.

On examination these patients are often described as tall and as having an increased lumbar lordosis This bodily build is by no means constant; any somatic type may be affected. The results of physical examination, except in the group who have chronic glomerulonephritis, are essentially negative

In the examination for orthostatic albuminuria, have the patient empty the bladder on retiring at night. The first specimen in the morning is collected, and this should be free of albumin. A second or a third specimen is obtained after the patient has been standing or walking for a half hour or more, and is examined for albumin. This specimen should contain albumin of grade 2 or more, graded on the basis of 1 to 4.

The diagnosis of orthostatic albuminuria is made when the results of general physical examination, including the blood pressure, microscopic examination of the urine and ophthalmoscopic examination are all within the limits of normal and the albuminuria occurs only when the patient is active and in the upright position.

Cylindruria. Urinary casts (cylindruria) are designated as hyaline, epithelial or granular, and as blood casts Hyaline casts, the commonest variety, are believed to originate in three ways. (1) from the renal epithelium itself, (2) from the coagulation of transuded plasma or (3) as an excretion of living tubular epithelium Epithelial casts may arise from the desquamation of the original lining of the renal tubules or from the shedding of newly generated renal epithelium. Blood casts are formed within the tubules from blood arising from a ruptured capillary, nearly always one of the glomerular capillaries

Hematuria, Pyuria and Bacteriuria. Blood, pus or bacteria may occur in the urine as the result of renal disease, but more frequently they have an extrarenal origin, such as from the renal pelves, ureters, bladder and urethra.

Renal hematuria indicates diseased glomeruli The glomerular disease may be a diffuse glomerulitis, or it may be the result of a focal embolic injury, or an infection associated with bacteremia, or from high fever

Idiopathic hematuria occurs in cases in which no discernible reason for the bleeding can be found.

Pyuria is much more often due to inflammation of the urinary passages than to a purulent inflammation of the kidney itself, though in surgical kidney and in tuberculosis of the kidney pyuria of renal origin is met with

Bacteriuria may have its origin in bacteria which pass through the injured renal filter. However, the usual cause is infection from below through the urethra or, sometimes, by direct passage from the rectum into the bladder.

Nonparasitic Chyluria. If the lymph channels are obstructed by inflammatory, suppurative or neoplastic disease in the lower part of the thoracic region or in the upper part of the retroperitoneal region, and if the dilated lymphatics rup-

ture into a kidney or a renal pelvis, chyluria ensues. Spontaneous chyluria may occur in the absence of any serious disease. Chyluria causes symptoms when the chylous masses obstruct urination The urine is milky with fat globules. The kidney and ureter which are involved are determined by ureteral catheterization, and the lymphatic connection is demonstrated by the retrograde urogram The Babcock test for fat in the urine may reveal the presence of as much as 1 or 2 per cent of fat

These patients may have ureteral colics from obstruction of the ureters by clots of the chylous urine. Likewise the urethra in men may become obstructed from clots Vesical symptoms may be severe until the clots are removed by endoscopic methods. If the condition progresses, these patients fail rapidly and die from innutrition

Tests of Renal Functional Activity. Richards and his associates demonstrated by direct analysis that the glomerulus in the frog is a mechanical filter and that the glomerular filtrate is a simple filtrate It seems likely that these same conditions prevail in man The maintenance of the composition of the extracellular fluids with its remarkably constant volume and composition of potassium, sodium, chloride and other electrolytes is accomplished by selective resorption by the renal tubules of exactly those constituents of the glomerular filtrate in the correct amounts to maintain a uniform composition of *the extracellular fluids of the body The constant maintenance of these uniform values* is made possible by the large total volume of blood flowing through the kidneys per minute (more than 1 liter) This is about one fifth of the minute volume output of the heart

Renal functions receive stimuli from other parts of the body, some of them probably in the form of hormones The pituitary body secretes an antidiuretic hormone that stimulates reabsorption of water Adrenal cortical hormones regulate the activity of the tubules with regard to reabsorption of sodium and potassium

The functional condition of the kidneys can be estimated by the specific gravity of the urine and by the urea and other clearance tests. Inability of the kidneys to concentrate the urine, as revealed by specific gravity tests, is the most practical and perhaps the most sensitive test of renal functional activity

Renal disease is not the only condition that can cause a decided decrease in renal function Any condition that causes a decrease in blood flow through the kidneys will cause a corresponding decrease in renal function Renal failure proceeds from (1) destruction of the nephrons by disease, as in chronic nephritis; (2) cessation of the renal blood flow from any cause, either by mechanical obstruction, as in sclerosis or thrombosis, or by excessive vasoconstriction or decrease in blood volume as is observed in shock, (3) toxic damage to the tubules, such as occurs in poisoning by nephrotoxic substances or by prolonged and severe ischemia, (4) fall in blood pressure in the glomeruli below 50 mm of mercury which results in a cessation of filtration and in anuria

It seems desirable to enumerate some of the special methods of testing clinically the functional ability of the kidneys Tests of renal function are performed under controlled conditions. Through these tests attempt is made to evaluate the ability of the kidneys to purify the blood by excreting (1) water, (2) the normal urinary solid constituents and (3) substances foreign to the body introduced especially for testing purposes In these studies special attention is paid to (a) the time required for the appearance of the excretion of the substances under test, (b) the length of time taken after excretion of the substance begins until all that is to be excreted has passed out, (c) the quantity of the introduced substance which can be recovered from the urine during the period of the test, (d) the concentration relations of the substance in the urine and (e) the relations between the amount of the substance in the blood and the amount excreted in the urine at the time of the test

Of the methods which determine the excretion of water and the excretion of total solids and of electrolytes, the determination of the specific gravity of the urine is most valuable diagnostically. If the specific gravity of a single specimen of

urine is more than 1.020, and if the urine is not heavy with albumin, generally the renal function is adequate for most immediate needs. However, if more information is required, it is well to use one of the procedures for concentration of the urine.

THE CONCENTRATION TEST OF ADDIS AND SHEVKY. 1. The patient abstains from fluid approximately 24 hours (after breakfast of one day until arising the next day).

2. Urine voided during the first 12 hours is discarded.

3. Urine voided during the last 12 hours (8 P.M to 8 A.M) is collected and the specific gravity determined. With restriction of fluid the normal kidney can excrete a urine of specific gravity of 1.025 or higher.

The specific gravity is a measure of the concentration of the dissolved constituents and is an expression of the contributions of each of the individual components of the urine. In a person who has normal kidneys and who is eating a mixed diet, the dissolved materials which are responsible for the specific gravity of the urine are the chloride, urea, sulfate, phosphate, bicarbonate and creatinine, named in the order of maximal contributions of each substance. The remainder of the specific gravity is the result of the contributions of organic compounds besides urea

Urines of low specific gravity from normal kidneys are the result of dilution. In advanced renal insufficiency the specific gravity of the urine becomes fixed In both dilute urines and those with a fixed specific gravity the relative composition is not altered from normal

In tubular disease or when there is reduction in renal mass, the specific gravity falls proportionately and finally becomes fixed at approximately 1 010 When the urine is heavy with albumin, correction for the albumin should be made by subtracting 0 003 from the specific gravity for each 1 gm. of albumin per 100 ml of urine.

In contrast to the concentration tests are those of dilution of the urine In these dilution tests the specific gravity of the urine should go down to 1.005 or less The capacity of the kidney to form a dilute urine parallels its concentrating powers sufficiently closely that dilution tests are seldom necessary. However, if a dilution test is desired, the test devised by Fishberg is a desirable one

THE DILUTION OR WATER FUNCTION TEST OF FISHBERG 1 Omit breakfast For dinner and supper give the usual routine nephritic diet or the diet to which the patient has been accustomed. Permit one glass of water after supper.

2 At 8 A M have the patient empty the bladder and give 1,500 ml of water. Discard the urine

3 Collect urine in specific containers at hourly intervals, beginning at 9 A.M and ending at 12 M, making four specimens in all

4 Carefully measure and take the specific gravity of each specimen

Methods which determine the power to excrete specific chemical substances, for instance phenolsulfonphthalein, have been and still are profitably employed in renal diagnostic work Forty to 60 per cent of the dye is excreted during the first hour and 20 to 25 per cent is excreted during the second hour by normal kidneys

THE UREA CLEARANCE TEST 1 This test is usually performed in the morning, since excretion is less likely to fluctuate during this period than at other times of the day, but, if necessary, it may be done at some other time, provided at least five and a half hours have elapsed since the preceding meal It is advisable for the patient to rest in a reclining position

2 The patient is requested to drink a glass of water and immediately thereafter empty the bladder This specimen is not saved but the time of voiding is carefully recorded.

3. At the end of approximately one hour, the patient again voids, the time is accurately recorded and the specimen saved At about this time (± 15 minutes) blood is withdrawn from a vein (2 to 3 ml is sufficient).

4. A second glass of water is then taken

5. One hour later the patient again completely empties the bladder The time is again accurately recorded and the specimen saved

The two specimens of urine and the blood are then sent to the laboratory for analysis

In Van Slyke's urea clearance test the average normal adult excretes the amount of

urea contained in 60 to 95 ml. of blood per minute The average excretion is the urea in 75 ml. of blood per minute. Slight impairment of excretion of urea is that amount in 30 to 60 ml. of blood per minute Moderate reduction is 20 to 40 ml Maximal reduction is the excretion of the urea in 10 ml. or less of blood per minute This test is inaccurate in edema with relative oliguria. It may be abnormally increased during fever in young persons.

THE XYLOSE TEST. On the supposition that xylose is not metabolized, and on the fact that inulin is excreted by the glomeruli only, clearance tests employing these substances have been devised but not commonly used.

THE PHENOLSULFONPHTHALEIN TEST. The phenolsulfonphthalein test has been widely used as a test of renal functional activity. In places where laboratory facilities are limited and when economy to the patient is desired, it can be employed, and if extreme dehydration or edema is not present, it may give the desired information in regard to renal function.

1. Give the patient 300 to 400 ml (about 2 glasses) of water to promote diuresis. Smoking and the taking of coffee or tea should be forbidden at least 2 hours prior to, and during, the test.
2. Twenty minutes later have the patient empty the bladder and discard the urine. In case of necessity catheterize
3. Then inject intramuscularly exactly 1 ml of the sterile phenolsulfonphthalein solution If there is general edema, the solution should be injected intravenously.
4. Exactly one hour and 10 minutes later have the patient empty the bladder (or catheterize) and save the urine.
5. Exactly one hour later (2 hours and 10 minutes after the injection) have the patient empty the bladder (or catheterize) and save the urine

Send both specimens to the laboratory for an estimation of the phenolsulfonphthalein in each

In preoperative examination before any major surgical procedure there are measured (1) the amount of urine, (2) the acidity, (3) the specific gravity and (4) the concentration of the blood urea. If the operation is to be made on a kidney and the function of the other kidney is in doubt, the phenolsulfonphthalein output of each kidney is ascertained after intramuscular injection of a given amount of this chemical; in some cases *0 01 gm of phlorhizin is injected subcutaneously and the amount of sugar excreted* by each kidney is subsequently determined

INORGANIC SULFATES The retention of inorganic sulfates as manifested by an increased concentration of these substances in the plasma or serum often occurs before there are detectable changes in the values for the blood urea or changes for the clearance tests The normal range of inorganic sulfates (SO_4) is from 2.5 to 5 mg per 100 ml of serum

NONPROTEIN NITROGEN AND BLOOD UREA The concentration of the total nonprotein nitrogen in the blood of normal persons in the postabsorptive state varies between 25 and 40 mg per 100 ml After an excessive ingestion of protein a concentration of 45 mg per 100 ml of blood may be present The nonprotein nitrogen comprises the nitrogen contained in the urea, ammonia, amino acids, uric acid, creatine and creatinine, of which the urea is the most important

The concentration of blood urea in normal persons varies from 10 to 50 mg. per 100 ml of blood if the blood is drawn during the postabsorptive state The range of blood urea (from 10 to 50 mg per 100 ml of blood) corresponds to 5 to 23 mg of urea nitrogen per 100 ml of blood

In routine clinical work the foregoing values for nonprotein nitrogen and for blood urea may be considered indicative of normal renal functional activity in the [illegible] is likely [illegible] a history [illegible] erformed [illegible] who have hypertension or who have a history of nephritis and have albumin in the urine.

Hyperazotemia occurs in renal insufficiency and from extrarenal causes In view of the extrarenal factors the measure of the concentration of urea in the blood

alone cannot be entirely relied upon for the detection of slight renal insufficiency, for often the concentration of the blood urea will reach 100 mg. per 100 ml. of blood during dehydration without there being any detectable impairment of renal functional activity If the possibility of the presence of these extrarenal factors which may cause an increase in the concentration of blood urea be kept in mind, and ruled out, the retention of nitrogenous substances is significant. It does not matter whether the concentration of nonprotein nitrogen or of the urea nitrogen is determined; the information is essentially the same when interpreted with a knowledge of the respective normal ranges of concentrations in the blood.

Functions of Individual Kidneys. By means of ureteral catheterization the urine from each kidney can be collected separately, and thus the amounts of urine, and also the solid substances, excreted by each kidney during a given time can be compared The procedure is of especial value in surgical cases in which one kidney is so seriously diseased as to demand a consideration of nephrectomy. Before performing nephrectomy, however, the surgeon desires to assure himself (1) that the other kidney is present and (2) that it is still healthy enough to keep the patient alive

The Reaction of the Urine. The reaction of the normal urine is acid However, normal urine with an alkaline reaction may be excreted for short periods of time without changes in health

The reaction and the degree of acidity (pH) of the urine are often helpful in giving clues regarding the character of bacteria causing an infection. Moreover, there is a form of urinary hyperacidity of neuropathic origin in which there is no infection, though the symptoms may simulate those of cystitis

BICARBONATE AND RENAL REGULATION OF ACID-BASE BALANCE The important renal function in the regulation of acid-base balance is made manifest by the reabsorption of base (bicarbonate), the excretion of acid phosphate and other acidic anions, the synthesis of ammonia and the formation of citric acid The quantitative relationship between plasma bicarbonate concentration and the rates of tubular reabsorption and urinary excretion of bicarbonate indicates that there is a definite renal threshold for bicarbonate of approximately 25 millimols per liter of plasma Below this concentration of bicarbonate in the plasma the bicarbonate in the glomerular filtrate is reabsorbed at a rate which may be expressed as a linear function of the plasma concentration Under ordinary conditions in which there is a need for conservation of base, for practical purposes all of the bicarbonate (99 95 per cent) is reabsorbed. In contrast, in excess of base, bicarbonate excretion may be almost as nearly complete. The renal reabsorption and excretion of bicarbonate therefore constitute a primary mechanism whereby the body may defend itself against either loss or increase of its alkali reserve and thus may maintain its acid-base balance

These mechanisms are mentioned here because of their importance in maintenance of normal reactions of the urine

Renal Failure Years ago MacCallum taught that in renal failure there is a loss of functional units, the nephrons of the kidneys. This loss may be incident to degeneration of the glomerulus first, followed by secondary degeneration of the tubule, or the disease may begin in the tubule When a sufficient number of nephrons are destroyed, there is an ensuing hypertrophy of the remaining glomeruli and tubules Recently Platt has made observations on animals and has reaffirmed that in renal failure some nephrons

is increased.

The concentrating capacity of the normal kidney has a limit When the kidney is sufficiently diseased, it can excrete either a small volume of concentrated urine or a greater volume of dilute urine. In many instances, as renal failure approaches, it seems that a greater volume of dilute urine (polyuria) takes place. Platt has expressed the belief that a polyuria and a fixed specific gravity of urine in renal failure are evidence of

normally functioning nephrons, each one of which is excreting an excess of urea and osmotic substances An increase in the concentration of the blood urea in the presence of polyuria implies that the compensatory mechanism manifested by a polyuria is no longer an effective compensatory mechanism.

A diuresis may be induced from the ingestion of water In the normal kidney or in the failing kidney the diuresis is due either to a diminished reabsorption of water by the normal tubules or to an increased secretion by the hypertrophied tubules An assumption of this particular sort of function in the renal tubule does not deny the established fact of glomerular filtration but it does question the ability of the glomerulus to perform the whole task of forcing fluid and electrolytes out of the glomerular capillaries and pushing these substances down the renal tubule It is more reasonable to assume that a tubular secretion of some fluid is economically desirable and hydrostatically possible.

In renal failure due to intrinsic causes there is an inability to excrete an adequate volume of urine to carry away the metabolic waste products and excesses of electrolytes Such an inability may be due to an insufficient number of functional units even though remaining functional units have hypertrophied as a compensatory mechanism.

As renal failure develops, there is evidence of disturbances of both filtration and absorptive function of the kidneys

Edema of renal origin appears to depend on injury to the capillaries in the renal glomeruli and similar changes in all of the small blood vessels all over the body, resulting in their increased permeability Acute weakness of the myocardium may precede or follow these vascular changes (see Theories of Heart Failure, Chapter 10).

The edema of renal origin begins very often in the face, especially about the eyelids, and is thus in contrast with the edema in chronic heart disease, in which the influence of gravity and of distance from the heart is an important factor in the distribution of the edema to distant dependent parts, such as the legs, if the patient is ambulatory, and the back, if confined to the bed

The *edema which occurs in the later stages of vascular hypertension* is rarely due directly to the renal lesion itself, but may depend on a failing myocardium,, and is therefore a true *stasis edema* rather than a renal edema A true renal edema may occur, of course, if the vascular disease seriously injures the kidneys or if an acute nephritis is superimposed on the chronic glomerulonephritis

In many forms of renal disease, but by no means in all, the blood pressure is high, and this *arterial hypertension* is associated with *hypertrophy of the left ventricle*, thus a maximal blood pressure of 160 to 200 mm of mercury or more, associated with dislocation of the apex beat downward and laterad, is common

Uremia signifies the presence of excessive amounts of urinary constituents in the blood Excessive urinary constituents in the blood may arise from extrarenal causes as well as from renal disease *Extrarenal hyperazotemia* is an example of an extrarenal cause for an apparent retention of urea This condition is commonly observed in obstructions of the pylorus and of the upper portion of the small intestine. These extrarenal hyperazotemias in part result from dehydration and the loss of sodium chloride from vomiting, from aspiration through suction tubes, or from diarrhea

Uremia occurs in acute and chronic forms, and the symptoms therefore vary widely A large number of symptoms have been grouped under the heading of uremia, but rarely are all of them present in any one patient In uremia, symptoms referable to the nervous system are common and are the most prominent. However, uremia also affects the respiratory, the circulatory and the digestive systems

The origin of the uremic symptoms is not clear The idea that the concentration of urea in the blood is responsible has been abandoned

A *complete and sudden suspension of the excretory functions of both kidneys* resulting in anuria may occur spontaneously or after ligation of both ureters or removal of a solitary kidney by surgical operation Under such circumstances symp-

toms like those which occur in chronic uremia are not present. At first there are no symptoms to suggest the impending disaster, but after a few days the patient grows weak and becomes sleepless, and toward the end of a varying period of about 10 days he complains of dryness of the mouth and drowsiness Muscular twitchings set in, but convulsions do not occur The pupils are contracted The sensorium usually remains clear until the end, though some patients have terminal delirium The temperature is subnormal Headache, vomiting and the ammoniacal odor of the breath so characteristic of uremia do not appear in obstructive suppression of urinary excretion

One of the most constant symptoms in uremia, and often the first to be complained of, is headache, sometimes so severe that morphine may be required for its relief

Uremic dimness of vision and uremic amaurosis may occur independently of retinitis, choked disk, the concentration of blood urea and the degree of acidosis Scotomas may or may not be present. Tinnitus aurium and dizziness are common symptoms

Convulsions are rare, but they are a part of the nervous symptoms Uremic convulsions usually are preceded by headache, vomiting and dimness of vision and occasionally by an aura The convulsions begin by an initial tonic stage followed by clonic spasms and tongue biting The pupils are usually dilated, rarely contracted After the fit the patient may remain in coma for a time, or there may be simply a period of somnolence Repeated convulsions are common In many of these cases death occurs during a fit, if recovery takes place, transient to temporary blindness is a common sequel

In uremia temporary paralyses are common Uremic hemiplegia and uremic aphasia are well known, they are probably due to edema of the brain, for at necropsy no gross lesion is demonstrable except in the cases in which actual vascular lesions have complicated a uremic state

Aside from the coma which follows a uremic convulsion, patients suffering from uremia sometimes are subject to coma that develops gradually after a period of drowsiness and mental torpor Hyperkinetic phenomena such as twitchings and local spasms may accompany the coma. The breathing is often of the Cheyne-Stokes type, but such breathing is not diagnostic Instead of complete unconsciousness, they may be delirium, variable in degree Sometimes outspoken maniacal seizures are present or, in the more chronic cases, pathologic ideas, melancholic, religious, erotic or persecutory, may develop

The presence of anorexia, nausea, vomiting and hiccough are common symptoms Sometimes there is diarrhea Whether or not the stomatitis and the ulceration of the intestine, so often found at necropsy on subjects who died of uremia, are due to the uremic intoxication or to complicating infection is not known

In uremic states inflammations of the serous membranes are common, for instance, pericarditis and pleuritis Peritonitis, however, rarely occurs. Often none of these is diagnosed clinically.

Myocardial insufficiency, hypertension, paroxysmal dyspnea and perhaps congestive heart failure are not uncommon in uremia.

At the onset of uremia there is a diminution in the amount of urine excreted, without a change in urinary specific gravity, which is low. The concentration of the total nitrogen of the urine and the urea nitrogen is decreased The acidity of the urine is increased, and the output of ammonia in the urine is relatively high The excretion of sodium chloride may not be changed Owing to the increased concentration of urea in the blood there is an increased excretion of urea through other emunctories, especially through the sweat. Fine crystals of urea may be visible on the skin of a uremic patient who has a dark complexion

The *diagnosis* of uremia is obvious if the history of the patient is well known so that appropriate chemical studies of the blood can be made (increased concentration of urea and nitrogen in the blood). The diagnosis of uremia may be difficult in those manifesting convulsions, paralyses, or coma when first seen. Likewise a patient manifesting some one particular symptom, such as persistent vomiting, hiccough, or Cheyne-Stokes breathing, in the absence of other symptoms, may not be recognized as uremic at first, though the further course of the disease and determinations of the concentration of urea and nitrogen in the blood will make the condition clear. Uremic convulsions may occur in a patient in whom the concentration of blood urea is less than 100 mg per 100 ml of blood.

The outlook in uremia is always doubtful The patient may recover from an acute attack, and if the renal disease is an acute nephritis and ends in recovery, there may be no recurrence However, when a uremic attack has occurred in the course of a chronic renal disease, even though the patient recovers from the attack in which he is first seen, this will, sooner or later, be followed by others, and death will ensue.

In those who are severely dehydrated (extrarenal hyperazotemia), and who have moderately good renal reserves, appropriate parenteral administration of fluids will often give immediate relief (see Intestinal Obstruction, Chapter 13).

Congenital Malformations of the Kidneys. The kidney, the ovary and the mullerian duct arise from the urogenital ridge If there is a defective development, there may be an associated absence of the kidney, the uterus, and the vagina, and there may be a rudimentary ovary, all on the same side Certain irregularities of development may result in a supernumerary kidney either entirely separate (free) or fused with the homologous kidney When the supernumerary kidney is separated from the other kidney, its ureter may be separated from the other ureters and have a separate opening into the bladder. It often unites with the adjacent ureter before reaching the bladder A much rarer condition is duplication of both kidneys and ureters, which does occur occasionally. However, any number of kidneys from one to four may be present

The kidney usually conforms to the usual size, shape and form Its variation in size is often dependent on the health of the opposite kidney Physiologic or compensatory hypertrophy is the commonest cause of unilateral renal enlargement

There are many inconsequential variations in shape, in normal kidneys, such as superficial fetal lobulations, and the elongated and rounded kidney.

The variations in form resulting in fusion of the opposite kidney constitute *horseshoe kidney* A horseshoe kidney is one of the commoner renal anomalies, although it is not so common as double kidney The opposite kidneys may be connected with each other at the upper or lower poles Fusion of the lower poles is the usual type There are, however, various types of fusion of the isthmus

Horseshoe kidneys need not cause symptoms Hydronephrosis is particularly common in horseshoe kidney, owing to aberrant blood vessels, fascial bands or stricture. Infection often follows

The two kidneys may form an elongated mass, divided by a fissure or by deep lobulation Each kidney has its own pelvis, calyces and proximal ureter. The ureter from each kidney may remain distinct and open separately into the bladder. In other instances the ureters from the two fused kidneys may unite at any point in their course and have a common ureteral orifice in the bladder Double fused kidneys are often poorly developed The calyces are fewer than normal It is postulated that double fused kidneys become pathologic from ureteral obstruction due to vascular anomalies, aberrant vessels or fascial bands which produce hydronephrosis, infection and the formation of stones

In the presence of a unilateral fused kidney, often there is some defect in the opposite half of the urinary organs

The *ectopic kidney* and the *movable kidney* are examples of anomalies of position. An ectopic kidney is misplaced congenitally, and there are often other evi-

dences of anomalous renal development The movable kidney, however, a normal kidney in ptosis, the abnormal position generally being acquir

The ectopic kidney is fixed and has a short pedicle and a short ureter. supply is derived from the nearest source arising and passing directly to t kidney. The vascular pedicle and ureter are far too short to admit the presun the kidney was ever situated normally.

The ectopic kidney may be congenitally hypoplastic and associated with o opmental lesions in the urinary tract There may be associated anomalies in ductive organs—especially in connection with the müllerian ducts such as no the mullerian ducts—from bicornuate uterus to complete nonunion, with uterine tubes, absence of uterus, and absence of vagina

When the ectopic kidney is lower than normal, and on the same side as orifice in the bladder, the condition is called simple ectopy, in contrast wi *ectopy, in which the ectopic kidney is on the opposite side from the opening of* into the bladder.

The ectopic kidney may be separate from the normal kidney or may be f it as in fused ectopy. A fused ectopy may constitute all of the renal tissue t possesses

If renal function is adequate and if the ectopic kidney remains healthy, the is compatible with renal health However, in ectopic kidneys pathologic dis such as hydronephrosis and infection are likely to develop When the ectop obstructs the birth canal, obstetric complications such as dystocia, rupture of t and death may ensue An ectopic kidney in the pelvis, discovered on palpa resemble an ovarian cyst, uterine myoma, or retroperitoneal sarcoma Urograp be used in all cases of obscure pelvic tumors

The diagnosis of all of these malformations of the kidneys can be es by intravenous urography, pyelography and cystoscopy However, the may not be suspected and then may be discovered accidentally during a operation for a condition suspected of being a pelvic tumor associated internal genitalia Unless it can be established that the other kidney is pre capable of sustaining life, the ectopic kidney should never be removed

Congenital anomalies of structure include such conditions as hypopla genital hydronephrotic atrophy and congenital cystic kidney. These conditic lap with others such as ureteral obstruction and renal tumors so that differ on clinical data cannot be made

Atypical vessels, aberrant arteries that go to the upper or the lower common in kidneys that are normal otherwise Such aberrant vessels, w pass to the lower pole, may kink the ureter as *the kidney changes its positic* may thus cause renal pain and hydronephrosis.

The Heart and Blood Vessels in Relation to Renal Disease. In *gl nephritis* there may be hypertension, cardiac enlargement, and congesti failure.

Hypertension is present in one half of those who have acute diffuse glo nephritis and occurs at the onset of the disease. The rise in blood pressure always moderate

Cardiac enlargement in nephritis is mild. It appears early, probably w first week or two of the disease In the presence of pronounced congesti failure the heart is greatly enlarged. If recovery from the congestive failure a return to normal cardiac size is the rule. Occasionally cardiac enlargem sists despite normal blood pressure In these enlarged hearts there is hype as wall as dilatation of the left ventricle

The cardiac enlargement may be present in the absence of hypertension instances *the degree* of cardiac enlargement is out of proportion to the m vation in blood pressure and its brief duration Both cardiac hypertrophy and ... attributed to myocarditis associated with glomerulonephr

Heart failure usually begins with tachycardia, muffled cardiac tones, an apical systolic murmur, gallop rhythm and rales at the bases of the lungs. In some instances the failure is characterized by a sudden onset of dyspnea and orthopnea, progressing to acute pulmonary edema. Pleural effusion is common and is part of the general anasarca.

Low or inverted T waves in lead I and in the precordial leads are common electrocardiographic changes Prolongation of the P-R interval and the Q-T interval may be present.

Chronic Passive Renal Congestion. This is a common condition It is in the end a congestive failure of the kidney It occurs under all conditions in which there is chronic passive congestion of the organs due to venous stasis, thus it follows (1) cardiac decompensation, no matter what its cause Less frequent causes of stasis in the renal veins are (2) obstructions to the inferior vena cava above the level of the renal veins and (3) pressure on the renal veins themselves from any cause

In cardiac decompensation two factors are important (1) decreased arterial flow into the kidney and (2) lessened venous outflow from the kidney A decreased arterial flow causes glomerular congestion, with excretion of albumin Lessened venous outflow causes engorgement of the kidney In cardiac decompensation the entire kidney is engorged The kidney becomes somewhat enlarged, is dark red, and is firmer than normal Degenerative changes occur in epithelial cells of the renal tubules, but there are no actual inflammatory lesions

The urine is scanty and of darker color than normal It is turbid and concentrated, and deposits a red sediment in the cold The specific gravity may at first be high A moderate amount of albumin is present Casts are present, but they are relatively few since there is no marked degeneration or destruction of the renal epithelium A few erythrocytes and leukocytes are usually to be found in the sediment

When functional tests are made, the phenolsulfonphthalein output is usually reduced, and the concentration of urea nitrogen is normal at first If the congestion continues, the concentration of urea nitrogen increases, though not to so great a degree as is observed in nephritis with the same degree of albuminuria

Chronic passive renal congestion is not confused with an early nephritis because there are signs of myocardial insufficiency present such as dyspnea, cyanosis, edema, palpable liver, enlarged heart, and often cardiac arrhythmia. Present in these patients are the possibility and the probability of an accompanying renal failure too If cardiac compensation is restored and there is no renal damage other than chronic passive congestion, the urine will become clear again, more abundant, of higher color, and free from protein and casts Should the urine, however, remain abnormal, there is coexisting renal damage

Diffuse Arteriolar Sclerotic Renal Disease. Chronic renal atrophy resulting from diffuse sclerosis of the small organ-arterioles of the kidneys is characterized clinically by polyuria, slight albuminuria and cylindruria, and chronic arterial hypertension with cardiac hypertrophy Death occurs often after many years of fairly good health, from cardiac failure, cerebral apoplexy, uremia or a terminal infection.

The cause of the arteriolar sclerosis underlying the disease is poorly understood. The sclerosis is now usually thought to be due to renal ischemia The disease is common and is said to be commonest among those who lead the strenuous life The tendency to occurrence in certain families has been demonstrated by Hines and others There is a morbid heredity in many of these patients

In families in which both parents have or had hypertension the children in due time have high blood pressure In families in which one parent has or had hypertension one of every four siblings has hypertension All of this is compared with an incidence of 3 or 4 per cent in those whose parents did not have high blood pressure. Draper has emphasized the sthenic type (short, stocky, heavy skeletal frame, broad deep thorax and

marked tendency to obesity) as being particularly susceptible to hypertensive vascular disease

Because of the diffuse nature of the process involving the arterioles throughout both kidneys, some poison carried through the blood must be responsible Such a clinical impression is not supported by the demonstration of the presence of any toxin in the blood of these patients. Other faults of metabolism leading to intoxication, including intoxications depending on internal secretion, especially of the chromaffin tissue, may be important etiologically.

Disease of the afferent glomerular arterioles is usually associated with arterial hypertension Since the voluntary muscles comprise a large part of the weight of the body, Wagener and Keith performed biopsy of muscles and compared the degree of the arteriosclerosis with that observed in the retinas revealed by ophthalmoscopic examinations They found a close agreement in the degree of the arteriosclerosis According to Moritz and Oldt the *presence of arteriolar sclerosis in the small renal vessels is almost* invariably associated with hypertension The absence of renal arteriolar changes betokens an absence of hypertension. When the degree of retinal or renal arteriosclerosis is great, arterial hypertension is invariably present, and renal insufficiency often develops

The structural changes in the renal arterioles, in the arterioles of muscle and in the retinal arterioles consist in a subintimal deposit of hyaline material As this increases in amount, the lumina become narrowed and atrophy of the muscular layer appears The glomeruli become shrunken or fibrosed or converted to hyaline masses, and the corresponding tubules undergo atrophy. Thrombosis of the arterioles, with or without *necrosis of the arteriolar wall, may be present In hypertension with renal insufficiency* Bell described the frequent occurrence of focal glomerulitis, an exudative and proliferative lesion in the glomerular capillaries.

Death from renal insufficiency in hypertensive disease occurs in only 1 of every 10 who have it. When renal failure supervenes in hypertensive disease, it may appear slowly over a period of years Occasionally, however, the onset may be rapid over a period of weeks or months. In these kidneys there are diffuse necrotizing arteriolar lesions characteristic of malignant hypertension and often associated with neuroretinopathy and hematuria

Those who die of renal failure incident to necrotizing arteriolar disease also have similar lesions in the gastrointestinal tract and other internal organs.

SYMPTOMS The onset is insidious, with polyuria and nocturia for a long time. The condition may be first suspected by the finding of albumin in the urine, in association with arterial hypertension at the time of a routine examination

As the disease advances, the symptoms are headache, nosebleed, insomnia, dyspnea, and symptoms of cerebral atherosclerosis such as forgetfulness and unreasonable behavior

If the patient, however, should give a history of transient edemas occurring *in* earlier life, especially in association with one infection or another, the possibility of the condition being an acute exacerbation of a chronic glomerulonephritis is considered A more careful inquiry is made in regard to previous urinary symptoms and transient *edema of the face and the extremities at the time of or following* acute infections of the upper part of the respiratory tract.

In the later stages of arteriolar disease of the kidneys, uremia is common The patients begin to have headaches and visual disturbances often characterized by a *failure of vision due to a retinitis of hypertension* Frequently these patients first consult the ophthalmologist because of a failure of vision resulting from the retinitis The signs of uremia include nausea, vomiting, diarrhea and, toward the end, convulsive seizures, delirium and coma.

An occasional patient who has an approaching renal failure will have a rapid loss of body weight attended by minimal symptoms referable to the kidneys or to the heart On inquiry about the urine, the patient often is aware of having passed an abundant amount of clear urine. In some the symptoms of renal failure will commence with ureteral colic incident to clotted blood obstructing the ureter, as a

result of profuse renal hemorrhage in an occasional patient, particularly men, a clot of blood will obstruct the ureter and cause urinary obstruction.

EXAMINATION. As in essential hypertension, the patient may be of florid complexion, or pale and tense. Often there is excessive sweating but if the renal disease is advanced, the skin is dry.

Evidence of recent loss of weight is common The temporal arteries are often prominent and tortuous in appearance The radial arteries are thickened, tortuous and palpable and seem too long for the arm The pulse rate is increased, often it is from 90 to 100 beats per minute The systolic pressure may be very high, 200 to 250 or more, measured in millimeters of mercury, and 130 diastolic; pressures as high as 300 systolic and 160 diastolic are sometimes met with in this disease. The heart is enlarged The apex beat is displaced downward and to the left. On palpation the cardiac movements are felt as forceful and determined The rate is usually regular. The aortic second sound is increased. Often there is a soft systolic murmur, heard best at the aortic area

Edema is not present unless there is a beginning myocardial insufficiency. When the heart begins to fail, edema may appear, with orthopnea and gallop rhythm; the urine then may become scanty, owing to the superimposition of a renal stasis upon the renal atrophy due to the sclerosis of the arterioles.

There may be only a trace of albumin in the urine, indeed, at times, albumin as measured by clinical means may be absent altogether. There is very little sediment, though on centrifugation a few hyaline casts will usually be found and, occasionally, a granular cast and a few erythrocytes.

In the early stages of the disease, and when there is no cardiac decompensation, the specific gravity of the urine is often less than 1 020, or fixed at about 1 010. The concentration of the blood urea and results of the urea clearance test are normal Concentration of serum sulfates may be increased In the later stages of the disease renal functional activity is greatly reduced as determined by all tests. The greatest concentration of blood urea known (700 to 800 mg. per 100 ml. of blood) occurs terminally in this disease

DIAGNOSIS The hypertension and the ophthalmoscopic findings which differentiate arteriolar sclerosis from glomerulonephritis, and the hypertension and evidence of decreased renal functional activity render the diagnosis obvious.

A constant polyuria, with low specific gravity of the urine, a trace of albumin in the urine with a few hyaline casts, along with chronic arterial hypertension and hypertrophy of the heart, and a concentration of blood urea of more than 60 mg per 100 ml of blood make the diagnosis certain If the patient is seen for the first time only after cardiac decompensation has set in, there may be temporary difficulty in making the diagnosis, for the symptoms of the arteriolar nephropathy are then masked by those of the superimposed chronic passive congestion; moreover, *the attention is then likely to be directed to the congestive heart failure.*

The differentiation of the disease from chronic glomerulonephritis in patients less than 45 years of age may be difficult or impossible during life unless the earlier history of the patient is known The symptoms are practically identical in the two conditions, and, as far as the patient is concerned, it is a matter of indifference as far as length of life is concerned If the physician avoids excessive laboratory procedures, the patient will be grateful to him

Renal Atherosclerosis and Hypertension. In a series of 145 consecutive necropsies Richardson attempted to determine the incidence of lesions which might cause narrowing of the main renal arteries and their relation to essential hypertension Thirty-two of the patients had had essential hypertension and 113 had been free from hypertension In 25 of the 32 there was apparent stenosis of one or both main renal arteries by atherosclerotic plaques In 22 of them the plaques were confined to a short segment of each artery near the aorta, in 2 the plaque

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of the primary division was definitely stenotic. In 8 the plaques were associate
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and in 5 no nodular atheroma was discovered. In the remaining 7 of the 32 there
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clusion was comparable to that seen in essential hypertension in only 3 Accessory
renal arteries were present in 6 These data suggest that atheromatous plaques may
be capable of producing renal ischemia and consequent hypertension analogous to
experimental hypertension

Atherosclerosis of the Kidneys. The kidneys in atherosclerosis may be of normal size, slightly enlarged, or reduced in size, and they are firm Scattered over the kidneys are seen depressed spots corresponding to localized or patchy atrophy due to atherosclerotic disease of the vessels supplying the part The difference between the atherosclerotic process and that of the arteriolar nephropathy lies in the fact that the atherosclerotic kidney is affected near the renal vessels of a larger caliber In arteriolar nephropathy the small arterioles throughout both kidneys are involved, leading to an atrophy evenly distributed throughout the kidneys and always associated with similar arteriolar changes in the other organs of the body Usually, unless both atherosclerosis and arteriolar sclerosis are associated, the larger peripheral vessels, such as the radial artery, also are atherosclerotic

The cause of the atherosclerotic nephropathy is that of atherosclerosis in general, about which little is known.

There are usually no symptoms unless renal failure has begun The kidneys may for a long time be able to excrete a normally concentrated urine Errors in diet, exposure to cold, alcoholic excesses, or bad colds may cause the appearance of an increase in the albumin in the urine and the number of casts.

In atherosclerosis examination reveals radial and brachial arteries which are sclerotic, lacking in elasticity and tortuous, they therefore seem too long for the arms The blood pressure reveals a high systolic pressure (180 to 190 mm. of mercury), the diastolic pressure is 80 or at most 90 mm. There may be a rough systolic murmur over the precordium The heart is not enlarged

The urine may contain a trace of albumin, but it is often free from albumin There is generally some polyuria, and the specific gravity may be normal, or decreased and fixed. The sediment contains a few hyaline casts. A few erythrocytes can nearly always be demonstrated in the urine.

The slight polyuria, the cylindruria, the transient albuminuria, the peripheral atherosclerosis (thickened radial), and the signs of atherosclerosis elsewhere in the body often permit of a presumptive diagnosis. Usually the condition is not discovered until necropsy In this form of arteriosclerosis of the kidneys, renal decompensation rarely occurs unless there is cardiac decompensation or severe infections, surgical operation, or a serious accident.

Embolic Nephritis (*Acute Focal Glomerulonephritis*) There are forms of focal glomerulonephritis and of embolic focal nephritis in which there is evidence that only minute disseminated regions in the kidneys are involved, the rest of the renal structure remaining intact. These instances depend apparently on the lodging of the infective emboli, often of low grade, in the kidneys. One of the best known ... the embolic glomerulitis which occurs during the course of bacterial endo-

carditis in which single glomerular capillaries may be thrombosed at the site of embolic lodgment.

In focal nephritis there may be no symptoms referable to the kidneys except the changes in the urine (albuminuria, microscopic hematuria). Uremic symptoms do not develop, since a great deal of healthy renal tissue remains As a rule, edema does not occur, though fugitive edemas are sometimes observed. There is no increase of the blood pressure

When septic emboli reach the kidneys and cause an embolic focal nephritis, miliary abscesses may occur in the kidneys These are met with, for instance, in general staphylococcal septicemia and in bacterial endocarditis

The diagnosis is rarely made during life

Urinary Infections. Infections of the urinary organs in men, women and children are common and often heal spontaneously without producing known illnesses or leaving residua If they do not heal, they do varying degrees of injury to the urinary apparatus and the general health The general health may be regained but injury to the urinary organs may remain, and thus urinary infections tend to recur after remaining symptomless for years A urinary infection contracted by an infant girl, if it does not heal, recurs during childhood, reappears during the early period of womanhood as the pyelitis of defloration, returns during gestation, and thereafter again and again

Urinary infections are so common during infancy and pregnancy that they are designated as pyelitis of infancy and pyelitis of pregnancy They recur when resistance to infection is lowered, as after exposure to inclement weather, after surgical operations, and during any illness, even of brief duration The urinary tract is prone to focalize and harbor specific infections such as gonorrhea, tuberculosis and septicemias due to pyogenic organisms Urinary infections may occur in healthy persons when a virulent organism gains entrance and becomes focalized in the urinary organs

The common bacteria present in urinary infections are the Enterobacteriaceae (the entire group of organisms) They are gram-negative, nonsporulating rods whose natural habitat is the nearby gastrointestinal tract Urinary infections are often caused by the intestinal saprophytes, the escherichiae. The various gram-positive cocci—streptococci, staphylococci and pneumococci, especially the streptococci—are second in number and importance as agents of chronic urinary infections. Various unidentified diphtheroid organisms and degenerated forms are common in chronic infections. The gonococcus rarely invades the kidneys It causes urethritis and cystitis. The tubercle bacillus is not frequent, but when present it is significant.

The relative incidence of these various bacteria in the urine depends on unknown environmental factors which permit of collective and individual susceptibility. Their discovery depends on the astuteness of the bacteriologist in the selection of bacteriologic cultural methods For instance, some forms of streptococci exhibit cultural caprices and thus may be completely obscured by the more luxuriantly growing Escherichia or coliform bacilli

The *portals of entry* of urinary infections are as follows: urethra, extension from adjacent organs, spread through the lymphatics, hematogenous infections, and the ascending infections

The *female urethra* is constantly exposed to infection from vaginal discharges and anal secretions, from trauma of coitus and childbirth, and from irritation of clothing and the protecting pads used during menstruation. From the urethra, as an *ascending infection,* the organisms may invade the bladder and the upper part of the urinary tract The *male urethra* may be the portal of entry after it has been damaged by infections such as gonorrhea and after trauma and from catheterization In both men and women these infections may remain localized or become ascending infections

was confined to one renal artery immediately proximal to the bifurcation and in 1 the renal artery showed no narrowing in the main trunk but the inferior branch of the primary division was definitely stenotic. In 8 the plaques were associated with a generalized atherosclerosis, in 12 an atheroma was limited to the aorta and in 5 no nodular atheroma was discovered. In the remaining 7 of the 32 there were no sclerosing lesions of the main renal arteries. In the 8 with unilateral stenosis, which were included in previous numbers for various reasons, microscopic examination of the ischemic and nonischemic kidneys failed to show any difference between them. In 3 there was malignant hypertension Afferent arteriolar necrosis occurred with equal frequency in the two kidneys In 105 of the 113 without a history of hypertension the main renal arteries exhibited no lesions and in 8, atherosclerotic plaques were present; in 6 they were unilateral The degree of occlusion was comparable to that seen in essential hypertension in only 3. Accessory renal arteries were present in 6 These data suggest that atheromatous plaques may be capable of producing renal ischemia and consequent hypertension analogous to experimental hypertension

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There is a tendency for the symptoms of urinary infections to recur if the cause of the recurrence lies in mechanical imperfections such as congenital or acquired strictures, other congenital malformations, horseshoe kidney, or hydronephrosis. In others the cause for the symptoms to recur is hidden in residual foci of infection in the urinary tract, such as the periurethral glands Occasionally it has been thought to be due to distant foci in the tonsils, teeth and sinuses

The diagnosis of a urinary infection depends on the astuteness of the physician in the interpretation of the reports of bacteriologic cultural findings of the urine when correlated with the history and the findings on examination of the urinary organs.

Ascending Renal Infections. An ascending renal infection may be defined as an infection originating in the urinary passages distal to the kidneys and progressing upward until the kidneys become involved

Injury to the kidneys from an ascending infection is often difficult to differentiate as such since the kidneys are subjected to injury from various toxins present in the blood and to derangements secondary to circulatory and metabolic diseases.

Pyelitis. Acute or chronic pyelitis occurs in most instances when a pre-existing obstruction is present However, it may arise without pre-existing demonstrable obstruction The infection usually subsides without leaving any residua in the upper part of the urinary tract Even repeated attacks may disappear and leave no cumulative effect However, repeated infections may impair the ureteral musculature, obstruct portions that are normally narrow, impair renal function and advance to hydronephrosis and pyonephrosis.

In acute pyelitis there is an acute inflammation of the mucous membrane of the renal pelvis and calyces In chronic pyelitis, or pyelonephritis, there is a combination of infection and poor drainage, although in some cases there is neither hydronephrosis or evidence of ureteral obstruction Chronic unilateral pyelitis is often the consequence of a stone in the renal pelvis or the ureter.

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filled with pus or fluid The filled capsule may be large and palpable or small and impalpable

While pyelitis is essentially the same disease whenever it is present, various forms are described as follows

1 Pyelitis of Infancy and Childhood The generally accepted explanation of the susceptibility of females to pyelitis is that the urethra is constantly exposed to infection by soiled clothes, diapers, washcloths, and occasionally vaginal discharges Pyelitis in boys has some definite predisposing factor, such as a congenital malformation, or genital or general infection or metabolic disease such as hypoparathyroidism

The organisms present in pyelitis in infancy and childhood are coliform, gram-negative bacilli, streptococci and staphylococci

The tendency to recur is a significant feature of this infection in all age groups, but perhaps this tendency is most significant in children Some girls have recurring attacks all through infancy and childhood With puberty the attacks usually cease. However, before the young woman is 25 years old she may have hypertension. Arterial hypertension and urinary infection subject the young woman to excessive risks especially if childbearing is attempted

2 Pyelitis of Pregnancy In pregnant women and in nonpregnant women the normal vesical urine often contains gram-negative coliform bacilli, streptococci

Direct extension from adjacent organs is infrequent, and is not the mode of infection in the common urinary diseases. For example, a diverticulum of the sigmoid may form an abscess and rupture into the bladder, but this sequence of events is rare even in those who have a diverticulosis of the colon.

In *lymphogenous infection* the organisms follow the lymphatic structures along the ureters or blood vessels in their spread.

Hematogenous infections first reach the renal parenchyma. The characteristic hematogenous lesion is focal abscess, which is often bilateral and multiple The commonly blood-borne organisms which reach the kidneys are two, the staphylococcus and the tubercle bacillus

Tonsillitis or sinusitis is effective in lowering the general health and making the patient more susceptible to any intercurrent infection, whether it is in the urinary tract or elsewhere

The opinion has been expressed by Rosenow, Billings and others that a distant *focus of infection* such as the tonsils, teeth, sinuses or ears may originate urinary infection. In some particular types of urinary infection, such as chronic interstitial cystitis, active focal infections as well as other causes for poor health seem to play a definite role as causative factors of production as well as in maintenance of these conditions However, extraurinary chronic focal infections rarely are significant sources of urinary infection

Any part of the urinary tract or the whole system may be infected. Specific infections tend to affect particular organs Tuberculosis always first attacks the kidneys in women, the kidneys or the epididymides in men In septicemia (especially staphylococcal septicemia) the characteristic lesion is focal abscess in the renal parenchyma.

Urinary infection and varying degrees of urinary obstruction usually coexist If urinary infection does precede obstruction, it produces edema and thus hinders urinary drainage and causes stasis Stasis of urine prolongs infection and increases the amount of tissue damage. Spontaneous attempts to heal the inflammatory process by the host may cause scarring and stricture formation in the urethra and ureters The ureteral muscle is replaced by scar tissue, and strictures weaken ureteral peristalsis, resulting in hydro-ureter, hydronephrosis, and eventually, perhaps, pyonephrosis This is particularly true if the emptying power of the bladder is weakened and there is incomplete evacuation of the infected urine.

Urinary infection and stone often coexist The etiologic relationship between the two is not proved Their constant presence together is more detrimental to the urinary tract than the presence of either condition separately A stone acts as a foreign body, making it impossible to eliminate the infection as long as the stone is present

Urinary salts may be deposited on infected surfaces in the bladder or the renal pelvis. Such encrustations hinder or prevent healing of an otherwise simple urinary infection.

Many urinary infections are of insidious onset and follow an insidious course The symptoms consist of frequency, urgency and burning on urination In some the discomfort is situated in the urethra, while in others it seems to be in the bladder. The pain is worse just before and during micturation The passage of urine gives temporary relief. Urinary infections without apparent localization may cause fever, headache, chills, nausea and vomiting They often commence with or follow infections of the upper part of the respiratory tract If the infection is situated in the upper part of the urinary tract the chills may be severe and the fever high The [illegible] the heights attained by almost any other condition [illegible] ial hypertension Anorexia, [illegible] ns of disease of the upper part of the urinary tract.

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The fully developed pyelitis, pyelonephritis, and infected hydronephrosis terminates in pyonephrosis or contracted kidney In pyonephrosis the kidney and renal pelvis and the renal parenchyma all may be destroyed, leaving the renal capsule filled with pus or fluid. The filled capsule may be large and palpable or small and impalpable.

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and staphylococci. During the second trimester of pregnancy there are ureteral dilatation and hypertrophy, or perhaps ureteral atony, hydronephrosis, and usually displacement of the ureters which result in varying degrees of urinary stasis. As a consequence of urinary stasis an infection is prone to develop. The sequence of events in the development of this infection is the same in either pregnant or nonpregnant women The bacteria pass from the bladder and originate a ureteritis, or a pyelitis From a pyelitis may develop hydronephrosis, pyelonephritis, pyonephrosis, or renal or perirenal abscesses. If a fresh urinary infection develops during pregnancy, or a chronic one becomes active at this time the lesions may do more injury and may be followed by more permanently harmful sequelae in the urinary organs than would occur in the nonpregnant woman. Women who have had pyelitis in childhood may have a hypertension and a symptomless urinary infection which becomes evident after the advent of pregnancy These women often have a decrease of renal functional activity.

3 Defloration Pyelitis (Honeymoon Pyelitis) The pyelitis of the honeymoon is an acute urinary infection precipitated by the trauma of coitus It is an uncommon form of pyelitis

In former times there was an opinion held by some physicians that defloration pyelitis was of gonorrheal origin This pyelitis is not an instance of infection from a gonorrheal husband The wife's infection is not gonorrheal The wife usually has a chronic nonspecific urethritis or an infected periurethral gland which is traumatized by coitus and thus reinfects the bladder and urethra In many instances she has had pyelitis during childhood.

There is an occasional woman in whom coitus will cause an exacerbation of a chronic cystitis especially after the menopause

Symptoms of Pyelitis In children there are chills, fever, nausea and indigestion, and prostration There may be some discomfort in the side, with frequency and burning on urination. Between attacks most children are free from symptoms Months or years may intervene between attacks.

In women and men an acute pyelitis may or may not be accompanied by frequency, urgency or burning on urination There may be no symptoms other than fever However, generally there are chills, fever, and often pain in the flank passing downward toward the genitalia. During pregnancy pyelitis is the commonest cause of fever

Examination in Pyelitis The general examination is significant for the absence of physical changes Special examinations of the urinary tract also are often negative if no complications are present Between the attacks the patient seems healthy Examination of the urine between attacks may or may not reveal pyuria. Albumin and an occasional erythrocyte may be found

Local tenderness in the region of the infected kidney and the palpation of an enlarged, sensitive kidney, or hydronephrosis are helpful signs if renal complications are present However, these palpatory signs are not constant even if renal complications are present The blood shows the usual reaction to acute infection in an increase in the leukocytes

Chronic pyelitis is a common source of poor health, and the disease may be difficult to detect The urine may remain clear for a day or two after the onset of general symptoms, the temperature attaining 104 to 106 F (40 to 41 C). If the ureter becomes opened and the infected, purulent urine appears, the fever ceases This sequence of events is diagnostically suggestive of ureteral obstruction and pyelitis.

Diagnosis of Pyelitis The diagnosis of pyelitis is made on the basis of the symptoms of a urinary infection, as have been outlined, and the presence of pyuria, positive cultures of urine obtained from catheterized specimens. The disease should be suspected in pregnant women who have fever and in children who have fever,

chills, and pyuria with or without vesical symptoms As a rule, in all cases the acute symptoms last about a week The tendency to recur is great despite treatment.

Pyelonephritis. Pyelonephritis is originated by the infection of pyelitis extending into the renal parenchyma. Pyelonephritis may occur in an acute or a chronic form With acute exacerbations an acute pyelonephritis is manifested clinically by greater toxicity, higher fever, graver constitutional reactions than is observed in pyelitis The urine is heavy with albumin, and occasionally casts and blood may be present in the urine; at times there is renal insufficiency as shown by a decreased renal functional activity. If the infection involves both kidneys, the condition is more serious than if it is unilateral.

Pyelonephritis also occurs frequently in men who have an ascending urinary infection from any cause (commonly, prostatism)

SYMPTOMS. The general symptoms are chill, fever, anorexia, headache and prostration There may be nausea and vomiting There is discomfort or pain beginning in the lumbar region, crossing the flank and extending downward toward or to the external genitalia Burning and frequency of urination are commonly present. Severe dysuria may occur and the urine may contain blood.

Frequently there are no symptoms A functionless kidney may be revealed by means of an intravenous urogram which is made as a part of a general diagnostic survey for some indeterminate pain Often it is discovered that pyrexia of previously unknown origin is caused by a urinary infection Functionless kidneys may be found in a search for the cause of fever

Results of the general examination may be negative Examination of the urine reveals the presence of pus and usually albumin Additional examinations reveal the presence of decreased renal function and evidence of hyperazotemia The diagnosis is based on a finding of a decreased renal functional activity or a functionless kidney in association with the foregoing history and findings.

Pyonephrosis. In pyonephrosis of a single kidney the renal function in the kidney is for practical purposes abolished, the parenchyma of the kidney is liquefied, and the capsule and the renal pelvis are transformed into a cystic mass containing pus Two types of pyonephrosis, excluding those due to tuberculosis, are distinct: the acute and the chronic

Acute pyonephrosis develops suddenly, in the course of a few days. In reality, it is an acute purulent collection in an infected hydronephrosis. Although renal function is completely destroyed by the acute collection of pus, renal tissue remains and may be restored to function if the pus is drained away immediately

Often it is extremely difficult to connect recurrent attacks of pyelitis with those which have gone before It may be impossible even to suspect from the history or the symptoms that pyonephrosis has developed. During remissions the urine often is normal and sterile

On examination search is made for all possible foci of urinary infection, such as chronic urethritis or other chronic infection or renal stone, and for a congenital malformation causing obstruction to ureteral drainage

Chronic pyonephrosis is characterized by destruction of the renal parenchyma and reduction or complete destruction of renal functional activity. The symptoms are often not differentiable from those of chronic pyelitis.

On examination a mass often is not palpable Intravenous urograms reveal that the kidney is functionless, a state which should be confirmed by ureteral catheterization

The specimen from the kidney obtained through the renal catheter consists of pus only, such a kidney excretes little or no phenolsulfonphthalein. Occasionally a pyonephrotic kidney cannot be catheterized, the ureter having been completely occluded by stricture

Pyonephrosis may be present with normal and sterile urine in the bladder if the

ureter is completely occluded. In every case of recurrent pyelitis a complete urographic study is indicated

The diagnosis of pyonephrosis rests on the demonstration of a cystic mass in the place of a kidney by methods of the urologic examination.

Abscess of the Kidney. Abscess or carbuncle of the kidney is due usually to *Staphylococcus aureus*. It is always of metastatic origin, often being associated with boils or carbuncle of the neck or other superficial regions

The lesion consists of a large ulcerative area in the renal cortex. Generally there is also a perinephritic abscess There is present a furuncle or a recent history of furuncles or a carbuncle Then comes a sudden onset of pain in the region of a kidney, fever, and eventually the formation of a mass in the flank.

There is a tender mass in the flank with fever, prostration, and often clear urine, except perhaps for slight albuminuria as a result of the fever. Intravenous urograms and pyelograms may indicate a cortical renal lesion

Tuberculosis of the Urinary Organs. Urinary tuberculosis is almost always a hematogenous infection The common primary foci are the lungs, bronchial lymph nodes, or intestinal tract

In the kidneys a tuberculous hematogenous infection involves the renal parenchyma first, and the excretory ducts (the renal pelvis, ureter, and bladder) secondarily. This order of progression is in contrast to the ascending infections, for they first affect the excretory ducts, the urethra, bladder, ureters, renal pelvis and finally the renal parenchyma.

Renal tuberculosis is largely a disease of young men and women It occurs, however, in children, in adolescents and in the aged. The right side is more frequently involved than the left side.

Primary urinary tuberculosis may occur in the bladder, the tubercle bacilli having gained entrance through the urethra This is far from the rule, however, for tuberculous cystitis rarely occurs without older lesions in the kidneys or in the genitals in either women or men The primary lesion in the lungs, intestines or lymph nodes may not be demonstrated, for it often is very small and cannot be recognized, and may have never given recognizable symptoms

In men the urinary organs may be infected from some contiguous genital or other structure This mode of infection is rare in women

In the beginning, tubercle bacilli reach the kidneys through the blood stream. If large quantities of the bacilli are disseminated throughout the kidneys as well as the rest of the body, the renal disease is but a part of an acute miliary tuberculosis, which is fatal When there are fewer organisms and the resistance of the host is good, the result is localized lesions in the kidneys. If the vital resistance is high, these miliary tubercles in the kidneys may heal promptly Often only one kidney heals completely The unhealed kidney remains active

Once established, the renal lesion progresses The tubercles progress, necrosis sets in, the tissue breaks down, and cavities form with caseation and abscess The abscesses coalesce, forming large cavities filled with tuberculous pus This condition eventually leads to complete destruction of the renal parenchyma, with the transformation of the kidney into a tuberculous abscess This process may require years for completion Often the slow progression of renal tuberculosis is hastened by secondary pyogenic organisms. The symptoms then resemble those of acute pyelonephritis

In all renal tuberculous lesions, in either men or women, the upper and the lower ends of the ureter are commonly and often severely involved. The ureteral infection begins in the mucosa and progressively infiltrates the ureteral wall, which becomes thickened, nodular, and occasionally occluded, thus shutting off the kidney, which may have ceased functioning by the time the ureter has become occluded, producing the so-called autonephrectomy. The lower ends of nodular ureters can be palpated

Tuberculosis of the *bladder in women* is secondary to tuberculosis of a kidney, and in men, to tuberculosis of a kidney or an epididymis The vesical lesion usually begins as a few scattered tubercles around the affected ureteral orifice. In severe infections it

may be difficult to identify the ureteral orifices The infection extends to other parts of the bladder. Tubercles form, caseate, coalesce, and break down, forming large ulcers The bladder becomes contracted.

SYMPTOMS The symptoms of renal tuberculosis are characteristically chronic The average duration of symptoms, when these patients are first examined, has been about three years. The symptoms are vesical distress, pain in the bladder and kidneys, hematuria, low-grade fever, occasionally chills, and loss of weight.

Vesical discomforts are often the first and may be the only symptom of renal tuberculosis. There may be a mild burning sensation, frequency, nocturia and pain All symptoms are intensified by an attempt to empty the bladder Incontinence is common when severe advanced lesions are present The dysuria may be agonizing, particularly if complicated by a pyogenic infection and when there is advanced disease. Once the disease is established, the vesical symptoms are persistent, without remissions.

The renal lesion seems to progress silently, until an abscess ruptures into a renal calyx, producing hematuria and ureteral and vesical infection Often a dull ache in the renal region, due to formation of abscess, is the first noticeable symptom. A fever, with few or no urinary symptoms, may be the initial symptom In other patients microscopic hematuria may be the first symptom In some the symptoms may commence with bleeding which is grossly evident, and this may be the only manifestation of the disease.

In renal tuberculosis years may pass without constitutional reaction or loss of health. Some patients who have bilateral renal tuberculosis or tuberculosis of the remaining kidney live for years in comparative comfort In other patients renal tuberculosis may progress rapidly The fever is high, loss of weight is rapid, and there are nausea, loss of appetite, weakness and anemia

A more rapid course is often observed when there is a secondary renal infection due to the colon bacillus, the streptococcus or other organism In such event the symptoms resemble those of acute or subacute pyelonephritis

EXAMINATION. Routine physical and roentgenologic examination of the lungs will reveal active pulmonary tuberculosis if present.

The presence of *tuberculous foci around the ureteral orifice* is almost infallibly diagnostic if the examination is made by an experienced cystoscopist, especially if supported by other data, such as the finding of tubercle bacilli in the vesical urine and the obtaining of clear and normal urine from the opposite kidney.

A competent urologist may record that the ureteral orifice is buried in tuberculous ulcerations or granulation tissue, it may stand out prominently. The purulent urine may dribble from it continually There may be complete anuria, due to ureteral occlusion, as in autonephrectomy

In tuberculous renal infections the observation of an impairment of function indicates either considerable destruction of renal parenchyma or ureteral obstruction In either instance the disease is advanced In mild infections there is no impairment of function.

When it is impossible for the urologist to catheterize the diseased ureter, either the ureteral orifice cannot be identified in the mass of ulceration or the ureter is impassably strictured In such cases, if the healthy kidney is secreting normal and sterile urine, it is safe to conclude that the opposite kidney is the one which is involved This impression is confirmed by intravenous urograms, and the nature of the infection is established by isolating tubercle bacilli from the vesical urine.

Lesions of the bladder are the commonest cause of symptoms both before and after nephrectomy Tuberculosis of the bladder is almost always secondary to renal tuberculosis

DIAGNOSIS The tuberculous nature of the renal infection is established by recovery of the tubercle bacillus from the catheterized urine by smear, culture, or

guinea pig inoculation. The presence of a urinary infection may be evident because of the presence of symptoms from an active pulmonary tuberculosis, accompanied by pus and blood in the urine.

As a general rule, the presence of an active focus of tuberculosis in the lungs or elsewhere is a distinct contraindication to nephrectomy. The kidney is enlarged and palpable and the ureter is palpable in 1 of each 3 of those who have renal tuberculosis

After nephrectomy it is generally wise to leave the bladder undisturbed for a few weeks because the vesical lesions usually heal spontaneously after the kidney has been removed If vesical symptoms persist, the stump of the ureter is to be examined. Occasionally a pocket of pus is found in this functionless stump which is maintaining the vesical infection; generally, however, there is a deep-seated, exquisitely painful ulceration of the bladder which apparently defies all forms of therapy.

Bilateral Renal Tuberculosis. In a series of 204 cases of bilateral renal tuberculosis Braasch and Sutton found essentially the same clinical features, symptoms, and associated tuberculous lesions as in cases of unilateral infection. The disease is usually more severe, the associated lesions commoner, the vesical symptoms worse, and the prognosis less favorable than in unilateral renal tuberculosis

Bilateral involvement practically always eliminates the advisability of nephrectomy However, in bilateral renal tuberculosis nephrectomy may be advised when one kidney is functionless and transformed into an abscess, or if it is causing severe hematuria or pain

The general futility of nephrectomy in bilateral renal tuberculosis is illustrated by the studies of Emmett and Kibler and by Braasch and Sutton If the remaining kidney is definitely tuberculous, as shown by the presence of pus and tubercle bacilli in the urine obtained from the ureteral catheter, the prognosis is definitely poor, and the outlook depends on the degree of renal involvement Even in those who have only a few pus cells, without demonstrable tubercle bacilli, the prognosis is worse than if the remaining kidney is normal In those who have tubercle bacilli and more than 10 leukocytes per high power field in the urine from the remaining kidney, the mortality rate is 100 per cent within 10 years subsequent to removal of the more severely infected kidney

The results of medical therapy were reviewed by Braasch and Sutton Of a group of 167 patients suffering from bilateral renal tuberculosis, who were not operated on, 72 per cent lived for 3 years or more, 58 per cent, for 5 years or more, 26 per cent, for 10 years or more, and 16 per cent, for 15 years The chief complaint of those who were living after 10 or 15 years was frequency of urination, they were apparently in fairly good health

Renal Syphilis. The pathologist recognizes both syphilitic nephritis and syphilitic renal gumma Wile reported the passage of *Treponema pallidum* through the kidney and its recovery from the urine

The clinical diagnosis of renal gumma is not made during life, except at the time of surgical exploration, when the patient's infection is made evident by the presence of multiple gummatous lesions in a kidney determined by biopsy and histologic examination

Renal Actinomycos [illegible] infec-
tion There may be only o [illegible]
The infection is general [illegible]
[illegible] the lesions about the head and neck [illegible] facto-
[illegible] e

may be accidentally [illegible] The abscess
periods of time and even after a large part of the parenchyma is involved

look like focal suppurative lesions caused by *Staphylococcus aureus* They may be dispersed or grouped, as in the so-called carbuncle.

The early symptoms often are pain, fever and leukocytosis The fever may appear early, may be of an intermittent type, and therefore may resemble that observed in an ordinary urinary infection Hematuria is not constant Symptoms of cystitis often occur.

The diseased kidney is usually palpable Urographic examination reveals deformity of the pelvis which is not characteristic If there has been a surgical trauma to the kidney, there is a definite and peculiar tendency of the incision to break open after healing seemingly has taken place Pus from the incision should reveal actinomyces when examined directly.

Except in generalized actinomycosis the diagnosis is often made after the kidney has been removed surgically or at necropsy Hunt and Mayo have successfully removed actinomycotic kidneys Antibiotics are now used in treatment of many patients who have these infections

Blastomycosis. Blastomycosis of the prostate, urethra, vulva, bladder and kidney has been recorded by Lewis, Carroll and Stryker and others. Often blastomycosis of these regions is associated with lesions of the skin Examination reveals dermal lesions or a chronic ulcer of the leg from which blastomyces are obtained by examination of the exudate from the ulcer or from the urine and by culture.

It may be difficult to prove pathogenesis of these organisms In urinary infections the organisms are abundant and easily found in the urine

Urinary Stones and Their Location. Urolithiasis is most commonly a disease of adult life except in disorders of calcium and cystine metabolism In these metabolic disorders stones may appear in the kidneys or ureters of children and youths.

Etiology It is generally impossible to point out the specific cause in any certain patient who has urinary stones Clinical experience seems to imply that urinary infections and subsequent changes in the physicochemical characteristics of urine, enhanced by obstruction, prolonged recumbency, climate, water, disorders of endocrine glands (parathyroids) and disorders of metabolism affecting cystine, uric acid and calcium may predispose to stone formation Likewise congenital malformations often seem to predispose to stasis of urine and stone formation More recently the formation of renal stone has been attributed to the diet

Much has been said about the etiologic importance of foci of infection in organs such as the teeth, tonsils, sinuses, ears or uterine cervix in the formation of urinary stones affecting and infecting the urinary organs As a result of these injuries stones form in the urinary passages Proof of this hypothesis is not yet available Nevertheless, all infections, remote and local, in those who have urinary calculi or in those who do not have urinary calculi, should be removed to improve poor health or to safeguard good health

Randall has summarized some of the possible effects of infection on formation of stone (1) It disturbs the colloidal balance (2) Infection produces epithelial or bacterial clumps, which may cause crystallization (3) Infection may cause papillitis (4) Bacteria have been found in, and recovered by culture from, the centers of urinary stones. (5) Urea-splitting organisms alkalize the urine and precipitate alkaline salts In addition, infection causes stasis by weakening the ureteral musculature and causing ureteral stricture It also may so damage the kidney that the kidney cannot excrete normal urine In urine which is culturally sterile the factor of urinary infection cannot be ruled out Sterile cultures are occasionally obtained from purulent urine and from subepithelial inflammatory lesions, for example in Randall's subepithelial plaque in the renal calyx.

Urinary obstruction slows the flow of urine, interferes with peristalsis, and prevents the expulsion of small solid particles of organic material which might develop into calculi

Prolonged recumbency is occasionally associated with the formation of renal or vesical calculi, especially if the cause of confinement is some chronic infection and especially a bone disease

Kimbrough, Denslow and Worgan reported the occurrence of urinary calculi in 15 of 800 young recumbent patients, immobilized for long periods for bone injury The incidence of such a small percentage (2 per cent) of calculus formation in such a large number of hospitalized patients with similar injuries under almost identical management makes it evident that there is a lithiasic diathesis due to general derangement of metabolism or local renal factors or both Reduced fluid intake, stasis and focal infections the writers considered to be the chief etiologic factors.

It has long been supposed that urinary stone is common in certain countries or districts, just as goiter is frequent in certain localities. Such a supposition is totally without foundation, for it is difficult to determine the incidence of urinary stones without the modern methods of examination, which have not long been in use

The cystine calculus is an unusual type of urinary calculi According to Joly, cystinuria is due to a congenital inability to metabolize proteins in the usual complete manner. This explains several of the clinical features of cystine lithiasis. it is occasionally familial, may occur in childhood, affects both kidneys, forms multiple calculi and recurs.

Uric acid calculi in gout constitute another example of calculosis in a metabolic disease. In gout the purine metabolism is disturbed, and uric acid is present in abnormally high amounts in the blood and urine, is deposited in various parts of the body and may also be deposited as calculi in the kidneys.

Albright and co-workers were the first to stress the significance and the frequency of the occurrence of renal stones in those who have hyperparathyroidism Hyperparathyroidism is a rare disease and therefore it cannot be, nor is it, a common cause of renal lithiasis. When hyperparathyroidism is the cause of renal stones they often are present *in both kidneys*

The dietary factor in lithiasis has recently attracted a great deal of attention Urinary stones have been produced experimentally in animals by feeding a diet deficient in vitamin A, but in clinical practice this fact has been of no value in the recognition or the treatment of lithiasis.

Prien studied various phenomena and mechanisms of calculogenesis from the standpoint of crystallography Pure calcium oxalate and calcium oxalate plus apatite, a complex calcium phosphate, were the substances most frequently observed in 1,000 human urinary calculi The nuclei of calcium oxalate monohydrate calculi are composed of that substance or of apatite. It is believed that some calculi originate from an attachment to the renal papilla, as described by Randall Not all calcium oxalate monohydrate calculi originate in this manner, those with a central nucleus and symmetric, concentric layers are believed to originate by crystallization from supersaturated urine No evidence is available to support the theory that foreign bodies, such as desquamated epithelium, act as the nucleus for renal calculi

Symptoms. A stone or stones *in the kidney* may cause *very little or no pain* A large stone (staghorn stone) may fill the whole renal pelvis and most of the calyces Often the stone causes nothing more than local irritation Often a large stone of this type is discovered when investigation is made to find the cause for pus and blood found in the urine on routine examination However, at any time there may be dull or sharp pain of any degree of severity which develops as the result of urinary obstruction caused by some complication produced as a result of the stone The discomfort is usually in the lumbar region and often extends down into the iliac fossa, external genitalia or even to the inner surfaces of the thighs

When a stone enters and obstructs the *ureter*, there are spasm, peristalsis and renal or ureteral colic Ureteral calculi often produce severe colicky pain situated along the course of the ureter. This pain may be so severe that moderate doses of opiates will not bring relief Nausea, vomiting and prostration accompany it

the calculus moves along, the movement is accompanied by pain. As the cal- nears the bladder, vesical symptoms become evident. There is frequency or difficulty in voiding Occasionally the descent of the stone from the kidney to the bladder can

almost be followed by the situation of the pain and the beginning of vesical symptoms Very small stones can be passed without causing symptoms. The amount of pain and the probability of passage of a stone depend on the relative size of the ureteral and urethral lumina and the diameter and smoothness of the stone. In a very narrow ureter a stone not more than 2 or 3 mm in diameter may cause severe colicky pain; in a normal elastic ureter such a stone might not cause any symptoms

The dilated, atonic ureter cannot contract vigorously, and hence in such a ureter a calculus may cause only slight pain or no pain at all. The stone may become embedded in the ureteral wall, further lessening the chance of its ever being passed

Experience teaches that ureteral calculi may cause obscure general symptoms over a period of years. These general symptoms may resemble those of an irritable colon In other instances there is flatulence, loss of weight, low-grade fever and occasional sharp discomforts that may simulate appendicitis, gallbladder disease or some pelvic disorder.

Vesical calculi are uncommon in women In men who have urethral obstruction, usually from prostatism, vesical calculi are common These stones, like renal stones, may cause very few symptoms. Symptoms when present are an intractable cystitis and hematuria There may be difficulty in starting the stream of urine, owing to the valvular action of a stone which may partly occlude the internal urethral orifice. In prostatism this may not be differentiated from the difficulty that is normally present During the passage of ureteral or urethral calculi general symptoms such as nausea, vomiting and prostration are prominent

EXAMINATION. The general examination of the abdomen, back and external genitalia is of value because of the characteristically almost uniformly negative findings.

The urologists may desire one or all of the following measures: intravenous urograms, cystoscopic examination and ureteral catheterization Intravenous urograms are rarely conclusive, and often a cystoscopic examination for inspection of the bladder or for the insertion of ureteral catheters is required

Ureteral catheterization may reveal a stone in the ureter which prevents passage of the catheter, or the catheter may pass by the stone With the catheter in place, the pyelogram then shows that the stones are in the renal pelvis However, stones in the renal pelvis do not give colics until they attempt to descend the ureter.

DIAGNOSIS. If trained hands have performed the manipulations indicated and trained eyes have viewed the roentgenograms, the diagnosis, as of a stone in the ureter, is usually definite

The diagnosis of urinary calculus is inferred from the presence of the symptoms of stone, and often there is a history of having passed calculi previously The urine contains blood and often pus

The urologists always consi [illegible]
passing spontaneously or after [illegible]
possibility cannot be formulate [illegible]
stone to pass if the stone is not more than 5 or 6 mm in diameter; fairly often stones of much larger caliber can be passed If the patient habitually passes ureteral stones, the ureter may become dilated and allow large stones (1 cm or more in diameter) to pass A ureter that is pathologically constricted or has a narrow lumen may catch a stone less than 3 mm in diameter Such a stone eventually may completely occlude the ureter.

The *situation* of the stone influences the decision as to whether or not the stone will pass A stone is more accessible to surgical intervention when it is in the abdominal part of the ureter When it is in the juxtavesical part of the ureter, it is difficult to reach surgically but is more accessible to cystoscopic manipulation.

The composition of a stone influences the decision as to whether or not the stone

will pass. If the stone is present in a gouty patient and therefore possibly composed *of uric acid* and *not obstructing the renal pelvis or the ureter*, a trial at dissolution may be made by alkalizing the urine by drugs or by placing the patient on an alkali-ash diet. In those who have cystinuria and no obstruction of the ureter treatment *similar to that employed in the case of uric acid stone* may be employed

If the urologist reports the presence of hydro-ureter or hydronephrosis, if there is anuria from the affected side, and if there is decreasing renal functional activity, the stone irrespective of its *composition should be removed immediately by the* simplest possible means

Small calculi in the renal pelvis or calyces remain in a calyx for months If there is a urinary infection and if the stone is of the borderline size which may not pass, and if it shows no tendency to leave the kidney, pyelotomy may be considered If there are neither symptoms nor infection, the stone should not be disturbed

Vesical stones are diagnosed by the roentgenologist and on endoscopic examination.

The Nephritides. Febrile *Albuminuria.* In the presence of fever, arising from an acute infection, of thermal origin, or developing after exposure to the wet and to cold air, there may be a mild albuminuria Often too there are casts in the urine In severe infections, such as lobar pneumonia, blood casts and albumin in quantity may be present Most of these albuminurias cease to be manifested when the infec*tion is over. In some, if a sufficient amount of renal damage is sustained, the condi*tion does not clear up It remains silent until a future date, at which time its recurrence is then recognized as an acute exacerbation of a chronic glomerulonephritis

Febrile albuminuria *usually is not of important significance It may* be a so-called glomerulitis or it may indicate only a parenchymatous degeneration of the epithelial cells of the tubules It is the condition which has been termed cloudy swelling of the kidneys by the pathologist in those who have died of acute infections In some instances, when there are certain advanced demonstrable degenerative changes in the epithelium of the renal tubules, particularly fatty deposits, it is called lipoid nephrosis. No such diagnoses can be made clinically, but these possible pathologic changes are to be kept in mind to be distinguished from the acute glomerulonephritis that sometimes complicates acute infections Often time and repeated urinalysis are required after an acute infection has subsided before differentiation of these various *conditions arising from fever can be made*

Glomerulonephritis. An advancement of the changes in the kidneys or the processes which constitute a febrile albuminuria constitute a glomerulonephritis This is particularly true if the febrile disease is due to group A streptococcus, for instance scarlet fever or one of the acute respiratory infections

Glomerulonephritis may follow infections such as pneumococcal pneumonia, staphylococcal and streptococcal infections, diphtheria, influenza, smallpox, measles and rheumatic fever A glomerulonephritis initiated by any one of these *infections* conforms well to type once the acute phase or, in some, the nephrotic phase, has been passed and the glomerulonephritis is established

The consensus at present is *that all instances of chronic glomerulonephritis* have originated as acute glomerulonephritis If this is correct, then the cause of both conditions is the same The chronic glomerulonephritis was once acute but has progressed steadily, or through a latent period, into the chronic phase The recorded proportion of instances of re [illegible] chronic varies in different studies of series [illegible] Many individuals have acute [illegible] medical advice is not sought

The association of glomerulonephritis with infection is not a cause-and-effect sequence Bacteriologic inquiry does not reveal an actual invasion of the kidneys

by the infectious organisms If a nephritis is present it may not be detected owing to the febrile albuminuria or acute cloudy swelling of the kidney.

Acute Glomerulonephritis. The term acute nephritis often includes and is synonymous with acute diffuse glomerulonephritis, acute focal glomerulonephritis, and an acute exacerbation of a chronic diffuse glomerulonephritis.

Acute glomerulonephritis is a sequela in most instances of acute infections by the group A streptococcus. The common infections predisposing to acute glomerulonephritis are infections of the upper part of the respiratory tract, tonsillitis and scarlet fever.

It seems likely that a toxemia from a streptococcal infection, without actual localization of the streptococci in the kidney, can cause the disease Microorganisms other than streptococci, or their toxins, may sometimes be responsible (see Chapter 18).

The height of infection occurs when the concentration of toxins is the greatest The acute nephritis develops during or after convalescence from the infection This time relationship suggested to Leichtenstern the possibility that glomerulonephritis is induced by an immune reaction resulting from infection, and this is as good a postulation as many of those which have been proposed

PATHOLOGY Owing to the presence of certain pathologic findings in the kidneys, many forms of acute nephritis have been described The nephritides which have been attributed to infections have been designated as bacterial, catarrhal, clostridial, croupous, desquamative, diffuse, exudative, focal, pneumococcal, suppurative (staphylococcal), acute suppurative (tuberculous), chronic syphilitic, and trench

The nephritides which are thought to have originated from a toxic substance, probably due to some sort of chronic anaphylactic reaction, include the acute, subacute, latent and chronic forms of glomerulonephritis.

The nephritides due to toxic chemicals are extensive but only the saturnine nephritides, due to lead poisoning, and those due to mercury have received special names The rest are simply designated according to the chemical agent, for instance, tartrate nephritis

The nephritides arising from causes definitely extrinsic to the kidneys and involving the kidneys secondarily have been designated according to the prevailing condition, for instance, azotemic, chloro-azotemic, dropsical, gravidarum, and transfusion nephritis.

There are the nephritides of a chronic nature, progressive and of a more ill-defined etiology than the acute nephritides, which have been designated chronic interstitial nephritis This form of nephritis formerly was thought to be due to any one or to all of several etiologic agents, namely, lead, alcohol and gout, or to be due to an acute nephritis which produced interstitial changes resulting in a decrease of size, the formation of cysts, and an adherent capsule In chronic interstitial nephritis the interstitial tissue increases, and a thickening of vessel walls and the malpighian corpuscles ensues Other names for this form of nephritis are chronic diffuse nephritis, arteriosclerotic kidney, senile kidney, small granular kidney, and small red kidney The term parenchymatous nephritis in contrast to chronic diffuse nephritis, indicates the main changes to be in the renal parenchyma This is the large white kidney of former times.

The foregoing terms are given in order to demonstrate that pathologists have been able to describe the degree and the kind of nephritis in a kidney very much more precisely than the clinician can relate to the pathologic findings the symptoms and the disease which proved fatal to the patient

In the acute nephritides, the common form which follows scarlet fever, the first changes are more interstitial than glomerular. The mildest form of acute glomerular nephritis is manifested by a swelling of the endothelial cells lining the glomerular tufts This stage is soon followed by avascularization of the glomerulus, with an infiltration of erythrocytes into the capsular spaces, necrosis, degeneration and exudation of granular [illegible] to albumin, which then accumulates [illegible] are polymorphonuclear neutrophilic [illegible] more prominent, and finally epithelial crescents are present in the glomerulus

Acute nephritis is commoner in young persons than in middle-aged and older

persons. Males are more often affected than females Pain is *not a feature of this* disease.

SYMPTOMS. Often within a month after an acute infection of the upper part of the respiratory tract, tonsillitis or scarlet fever, there appears edema, first of the face and about the eyes and the eyelids. The edema develops rapidly and is soon observed in the legs Sometimes the edema may be absent or fugitive or it may progress to a general anasarca and on occasion to pulmonary edema

Other symptoms that may be present include fever (*temperature, 100 to 102 F,* 37.7 to 38 8 C) and uremic symptoms. The uremic symptoms, consisting of headaches, dimness of vision, nausea, vomiting and insomnia alternating with mental dullness, vary greatly in severity, sometimes being so mild as not to attract attention. In other instances death from uremic poisoning ensues

A type of the acute glomerulonephritis of insidious onset sometimes complicates lobar pneumonia The onset may be so gradual as not to be noticed unless daily routine *examinations of the urine are made. There may be no edema in the* milder forms The symptoms of the nephritis are so trivial that they are lost sight of in the presence of the prominent symptoms of the primary disease.

EXAMINATION Edema is present, manifested first by puffy eyelids, pasty face and watery eyes Edema next appears in the lumbar region, and later in the legs. In a few cases edema appears before albuminuria or casts are found in the urine. The course of the disease and of the edema is variable

If uremia is present, there is urinous odor to the breath, and there are headache, drowsiness, and, sometimes, convulsions and coma The blood pressure is increased, the systolic pressure being higher than 150 mm of mercury, in about half of those who are examined Tachycardia or occasionally bradycardia, and dryness of the skin with pruritus are observed. A severe anemia is often of serious prognostic import Examination of the urine reveals oliguria, pollakiuria, hematuria, high specific gravity, albuminuria and cylindruria.

In estimating the damage that has been done to the kidney and the relative injury to the glomeruli in some instances and to the tubules in others, the methods of testing functional renal activity should be resorted to as they apply to the water intake and water output and the specific gravity of the urine. These functional tests are the concentrations of the blood urea, serum sulfates, creatinine, and the various clearance tests such as the urea, sulfate, creatinine and the clearances of certain sugars such as inulin Single determinations of the functional tests are of slight diagnostic and prognostic value It is the trend of repeated tests which is significant

DIAGNOSIS. In the acute nephritis of abrupt onset, for instance after scarlet fever, when there are rapidly developing edema, pallor, nausea, vomiting, increased blood pressure, hematuria and albuminuria, there can be no doubt as to the diagnosis It is in the forms of insidious onset that the possibility of the disease is to be remembered and recognized as such as quickly as possible The characteristic features of acute glomerulonephritis are edema of the face, anemia, hematuria, urinary casts and albuminuria In some the urea clearance is decreased and the serum sulfates are increased before hyperazotemia prevails

If the condition of the patient before the onset of the nephritis has been known, and especially if a record of the state of the urine previously is available, the changes in the character of the urine often will indicate the nature of the trouble.

In the differential diagnosis of acute nephritis it is necessary to distinguish it from (1) simple febrile albuminuria, (2) orthostatic albuminuria, (3) chronic passive renal congestion, (4) subacute or chronic glomerulonephritis, (5) amyloid kidney, (6) renal infarct, (7) *the different forms of pyelitis* and pyelonephritis, (8) renal tuberculosis, and often (9) from arteriolar renal disease

Latent Glomerulonephritis. About one half of those who have acute glomerulonephritis recover from the disease, and at the end of about 6 months no evidence

of the disease can be found There are an indefinite number in whom the disease seems to persist in a latent form For instance, there is a continuous excretion of abnormal amounts of albumin and numbers of erythrocytes, but renal function is preserved This period may last for months or even years Some patients may cease to excrete appreciable numbers of erythrocytes but continue to lose sufficient albumin in the urine to deplete the plasma proteins Finally, in some the nephrotic syndrome develops which is characterized by edema, massive albuminuria, low plasma proteins, elevated blood cholesterol, normal blood pressure, and normal or nearly normal renal function as measured by clearance tests In others there is a definite chronic glomerulonephritis on the first examination In still others it seems reasonable that recovery may occur after months of latency, but no proof of such recovery is possible

Subacute or Subchronic Glomerulonephritis There are no diagnostic criteria to separate subacute glomerulonephritis from latent or from chronic glomerulonephritis. There are no objections to these terms, if it is desired to use them.

Chronic Glomerulonephritis Chronic glomerulonephritis is a diffuse destructive process in the kidney causing deforming changes in the glomeruli, in the parenchyma and, to a less extent, in the interstitial tissue of the kidney The urinary abnormalities vary In some the changes are insignificant, while in others the urinary changes are almost diagnostic The urinary changes, edema, secondary anemia, and, usually, a fatal termination in one or two years are characteristic of an unmistakable clinical syndrome.

The cause is the same as that of acute glomerulonephritis

PATHOLOGY The kidneys in chronic glomerulonephritis are characteristically reduced in size, although this is not always the case, even at death the kidneys may be of almost normal size. The gross renal weight does not parallel the number of remaining functional nephrons Some nephrons are atrophic, while others are definitely hypertrophic, the hypertrophy affecting particularly the proximal convoluted tubule There is an increase in the number of vasa recta, that is, arterioles whose capillaries are distributed to tubules without the interposition of a glomerulus Some tubules whose glomeruli have been destroyed persist as aglomerular tubules The tubules have great power for regeneration and recovery wheras glomerular healing is difficult and uncertain

The early detectable change in the glomerulus is a hyaline change in the glomerular membrane After this is seen a proliferation of the endothelial cells of the capillaries or of the epithelial cells about the glomerular tufts The glomerular capillaries become obstructed and epithelial crescents form in the capsule The presence of hemorrhages and coagulated albumin varies with the acuteness of the process.

By the time death comes, there are widespread vascular disease, and enlargement of the heart Often death is due to congestive heart failure.

SYMPTOMS There may be only the symptoms of weakness and anemia accompanied by edema The edema may be slight at first, and just a little puffiness of the eyelids in the morning or of the ankles at night is all the patient has observed. Gradually, however, the edema increases The most extreme examples of anasarca are those due to glomerulonephritis The subcutaneous tissues all over the body are involved The dropsical fluids fill the serous cavities of the body. There are general weakness, and loss of appetite

Uremic intoxication of greater or less degree is nearly always present, though the symptom of edema is more obvious than are the symptoms of uremia The manifested uremic phenomena consist of headache, drowsiness and digestive disturbances. It is only occasionally that the severe uremic manifestations are present, such as convulsions, coma, uremic amaurosis, and mental disorders or psychosis

Other patients first come under observation with symptoms of an acute nephritis. They give a history of a recent tonsillitis or other infection On examination the urinary findings represent an acute nephritis, and only the presence of the combina-

tion of cardiac hypertrophy, anemia, retinopathy and low renal function indicates the existence of chronic disease.

In still other patients the symptoms of the acute stage evolve rapidly into a chronic stage. The edema subsides, but the albuminuria, hematuria, hypertension and diminishing renal function adversely progress. However, in the majority, a history is obtained that the symptoms of the initial stage subsided, the blood pressure returned to normal, and erythrocytes disappeared from the urine, although massive albuminuria persisted and the edema became pronounced. This so-called nephrotic *phase of glomerulonephritis may persist for months or years. Eventually the albuminuria* decreases and edema disappears, but hypertension becomes manifest and there is a progressive decrease in renal function These patients, however, may pass through or into a *latent stage* (latent glomerulonephritis) in which persistent albuminuria is the only recognized abnormality. Other patients continue to show slight or moderate elevation of blood pressure after an acute attack, with only a slight albuminuria For a long time, even many years, the clinical course in these patients closely resembles that of primary or essential hypertension.

Examination The blood pressure is not elevated to the degrees seen in arteriolar sclerosis and does not show the fluctuations which are characteristic of the early stages of this disease While systolic pressures of 250 mm. of mercury and diastolic pressures of 150 or more do occur in chronic nephritis, the more usual range is 160 to 180 systolic and 100 to 120 diastolic. As a result of the hypertension there is hypertrophy of the left ventricle, although there may be no dilatation or detectable cardiac enlargement Retinal lesions, with hemorrhage, exudate and papilledema occur The anemia tends to parallel the degree of impaired renal function. It is usually normoblastic in type, and counts of 2,000,000 erythrocytes in each cubic millimeter of blood and a concentration of hemoglobin of 40 per cent are common findings

The urine in chronic glomerulonephritis is usually increased in volume, amounting to 2 to 3 liters a day. The specific gravity is low, and the patient cannot excrete a concentrated urine during a concentration test In severe impairment the specific gravity becomes fixed within a point or two of 1 010, the patient being unable to excrete either a more dilute or more concentrated urine

There is usually a persistent albuminuria which, however, may be slight In contrast to the urine in arteriolar nephrosclerosis, there is a constant excess in the number of erythrocytes in the sediment The excess, however, may be *slight, and* only detectable by an Addis count Casts likewise are present, but may be scarce, particularly in dilute urine The number of erythrocytes increases during periods of activity or rapid progress of the disease

During the progress of the disease there are phases characterized by albuminuria, large number of casts, manifest edema, only slight hematuria, and no or only slight cardiovascular changes In about half of these cases arterial hypertension does not develop In rare instances there may be blood pressures in the lower limits of the normal range In the same cases, as the disease develops, the edema may disappear, albuminuria may decrease, hematuria increase, polyuria become marked, and there may be extensive cardiovascular changes and arterial hypertension

Whenever possible, tests of renal function should be undertaken, since they may reveal the state of renal compensation or decompensation, the relative degree of injury to the glomeruli, or of the tubules, and the progress of the disease *Of these* tests, those that measure the variations of the specific gravity of the urine, the urea clearance test and other clearance tests are the most desirable It is the general trend of the test that is the most valuable in determining the progress of the disease

Diagnosis The presence of albuminuria, hematuria, cylindruria, and oliguria, ... with edema, in a young patient who does not have cardiac decompensation,

makes the diagnosis of glomerulonephritis most likely. In the older patient (40 to 50 years of age) the distinctions to be made are often between (1) subacute diffuse glomerulonephritis and (2) acute diffuse glomerulonephritis, or (3) when an acute renal failure occurs as a part of an advancing chronic arteriolar sclerosis with hypertension The history, and the physician's knowledge of the previous condition of the patient and his urine, may well be diagnostically decisive In the absence of such knowledge there may be real difficulty for a time in arriving at a satisfactory differentiation between glomerulonephritis and arteriolar disease Hematuria is more constantly present in glomerulonephritis than in arteriolar disease

Wagener and Keith have expressed the belief that the differential diagnosis between chronic glomerulonephritis and arteriolar sclerosis with hypertension and renal failure can be made from the retinal changes present (see Hypertension, Chapter 10).

The Nephrotic Syndrome (Lipemic Nephrosis) The syndrome presents certain uniform and consistent features, such as gross edema, hypoproteinemia, hypercholesteremia, lipemia and heavy proteinuria in the absence of congestive heart failure. It is convenient from a clinical point of view to regard the syndrome as an independent entity Heymann and Alperin prefer the term "lipemic nephrosis with or without nephritis " This term keeps the nephrotic diseases in one group, separates them from chronic glomerulonephritis and does not imply the priority of the nephritic component It also alters the hopeless prognosis for chronic glomerulonephritis which has been observed in nephrosis with nephritis The nephrotic diseases have a different age distribution from that of acute hemorrhagic glomerulonephritis. The maximal disposition for the nephroses is found in the second year of life while glomerulonephritis is still rare The incidence of glomerulonephritis increases with age up to puberty, whereas the incidence for the nephrotic diseases decreases.

The etiology of the nephrotic syndrome is not known The syndrome is by some believed to be renal in origin, either a disease entity or a phase in chronic glomerulonephritis, while others believe it to be of extrarenal origin, caused by some disturbance of the protein metabolism

Lange and his associates believe the nephrotic state to be a generalized disease of the small blood vessels with a tremendous increase in capillary permeability The formation of edema, in their opinion, is due to this fact and not primarily to the lowered colloid osmotic pressure Preceding infections, which are observed in patients who have acute glomerulonephritis, are not regularly observed in children ill with nephrosis with or without nephritis

Janeway and his associates and Blumberg and Cassady noted a pronounced diuresis in children with chronic glomerulonephritis who contracted measles Seegal and Wertheim have stated, however, that in some patients the occurrence of an infectious disease in the course of the nephrotic syndrome may prove detrimental, inducing hematuria and further accumulation of edema. Patients with the nephrotic syndrome are lacking in resistance and usually die of an intercurrent infection It is also held that a specific fault in the renal excretion of sodium is the important factor. The alleviation of the nephrotic syndrome during various infectious diseases has frequently been observed Some believe that renal dysfunction in the disposal of water and electrolytes is chiefly concerned

Symptoms The onset is usually insidious, the patient feels weak and tires easily The fatigue may have begun weeks or months prior to onset of the edema, but the patient usually does not consult a physician until the edema becomes obvious. To the patient, the edema is the disease

In other patients there may be a history of sore throat or acute respiratory infection from which there was prompt and apparently satisfactory recovery Often the rapid onset of edema is preceded by a feeling of heaviness and stiffness in the extremities The edema soon becomes diffuse. The body cavities fill with fluid Shortness of breath follows. Usually there is no fever. The appetite is poor or absent.

EXAMINATION. The results of physical examination are negative except for the massive edema On examination soon after the appearance of the edema it is dependent, then generalized, and often associated with ascites and hydrothorax The edematous tissue is peculiarly soft, pitting easily on pressure. The amount of edema varies inexplicably at times, and cannot be correlated with changes in the concentration of plasma proteins or the amount of protein excreted in the urine.

The findings of hypercholesteremia and hyperlipemia on examination of the blood in the nephrotic syndrome are perplexing, for the fat content of the diet appears to have little influence on the plasma composition The subclinical forms of the nephrotic syndrome may be detected by the determination of the values for serum albumin and serum cholesterol An abnormally low concentration of serum albumin in association with hypercholesteremia may be evidence of the presence of the nephrotic syndrome.

The plasma protein composition is greatly altered in the nephrotic syndrome There is a significant reduction in albumin, while the globulin content may rise, especially in amyloidosis, may remain unchanged or may fall The urinary proteins are probably derived from plasma by a filtration mechanism The obvious site of this filtration is the glomerulus, indicating a defective glomerular activity, even though the glomeruli show little or no gross alteration. The urine is highly concentrated and contains cellular elements of casts of various kinds with little or no blood. Improvement in the patient's condition is accompanied by a decrease in urinary protein and an increase in plasma proteins

DIAGNOSIS. The diagnosis of the nephrotic syndrome is based on the presence of massive albuminuria, edema, and reduced concentration of protein in the plasma, with reversal of the albumin-to-globulin ratio, usually accompanied by an increase in plasma lipoids and a low basal metabolic rate If the disease long persists, hematuria or hypertension or nitrogen retention or all three tend to be present During the course of a chronic infection findings comparable to those of nephrosis may be indicative of amyloidosis

Lower Nephron Nephrosis. The term lower nephron nephrosis includes renal disease characterized by tubular degeneration and necrosis with subsequent regeneration, deposits of pigment in the tubules, and interstitial inflammation but no visible glomerular alterations The disease may be caused by a wide variety of agents which induce prolonged shock, renal ischemia and anoxia or allergic and toxic damage to the tubules Some of the best known causes are (1) extensive burns or wound shock, especially the crush syndrome, (2) hemoglobinuric nephrosis due to mismatched blood, (3) sulfonamides, (4) inhalation of carbon tetrachloride, (5) blackwater fever and other factors responsible for intravascular hemolysis of erythrocytes, (6) hyperthermia and various poisons and on rare occasion after transurethral resection of the prostate gland

The important features are the acute development of oliguria or anuria and hypertension, and the invariable danger and frequent occurrence of congestive heart failure.

The development of heart failure usually is precipitated by the parenteral administration of fluids in an effort to alleviate vomiting, promote diuresis or maintain fluid or electrolyte balance Intracellular breakdown may be caused by excessive administration of intravenous fluids; when present, such breakdown contributes to the excess of extracellular volume and edema Both of these factors are important because there is no urinary output or only an insignificant one Cardiac dilatation, gallop rhythm, pulmonary congestion and hydrothorax, subcutaneous edema and ascites are common Death is not common, but when it does occur it is often due to acute pulmonary edema as a part of the left ventricular failure

When the concentration of blood urea begins to decrease and diuresis is present, caution is exercised in pursuing any immediate urge in the restoration of acid-base

and electrolyte balance These measures are best undertaken slowly and preferably by oral administration of these substances. In most instances no therapeutic measures are necessary when the basic renal lesion is healed, renal function is restored and a normal diet is permitted. As a rule, lower nephron nephrosis is a spontaneously reversible condition in which diuresis begins 2 weeks after onset, independent of treatment

Amyloid Kidney. Amyloidosis of the kidney is a degeneration of the kidney in which amyloid is deposited in the organ, chiefly in the walls of the blood vessels, sometimes in the membrane of the renal tubules Amyloid disease is often a generalized process with similar deposits occurring in the liver, spleen, heart, intestine, skin and lungs as well as in the kidney

Amyloid deposit occurs in cachectic states due to chronic pyogenic infections, syphilis, or tuberculosis, and as a primary disease beginning insidiously. The diag- [illegible] in several organs. [illegible] one to occur may be [illegible] suppurative pyelitis, and bronchiectasis; furthermore, in chronic tuberculosis of the lungs, bones and joints, amyloid is common, and in tertiary syphilis it is frequently seen. In some instances suppuration does not precede the onset of symptoms of the disease. These are examples of primary amyloidosis (see Chapter 22)

When amyloid degeneration occurs in the kidney, the organ enlarges and the cortex broadens and grows waxy in appearance On section, the glomeruli stand out distinctly. If a little Lugol's solution is poured over the surface, the glomeruli and the walls of blood vessels and of tubules that contain the amyloid material stain a dark mahogany brown color

There are no symptoms characteristic of amyloid disease of the kidney. If, during the course of an illness which has been diagnosed as nephrosis, there is a sudden development of renal failure, and death occurs, the patient usually has had amyloid disease of the kidney Also it is to be remembered that amyloid disease can be implanted in a kidney that is already the seat of other forms of renal disease aside from nephrosis, such as arteriolar renal disease.

Usually albuminuria, cylindruria, edema and enlargement of the spleen and liver are present. Often there may be chronic suppuration, tuberculosis or syphilis Mild forms of the disease, however, and even many of the severer forms are not recognized until necropsy.

The diagnosis of amyloid kidney can be made if there is an abundant amount of urine, of low specific gravity, yet heavy with albumin These findings are present in the absence of cardiac and vascular phenomena of an arteriolar sclerotic kidney. When the foregoing findings are associated with an enlarged liver and spleen, or at least one of them, especially the spleen, and when at the same time there is present a chronic suppurative process, the diagnosis is made Amyloid disease is suspected if, in a patient who has chronic nephrosis, uremia suddenly develops and death ensues There are those who have chronic primary amyloidosis without any of the foregoing findings present The reaction to the Congo red test is positive in about 6 of every 10 of those who have amyloidosis This test rarely gives a false positive reaction

Renal Trauma. Renal injuries often are sustained from trauma to the lumbar region The trauma is followed by pain in the region of the kidney or the abdomen, shock, nausea, vomiting, and the passage of bloody urine. The degree of shock as well as all other manifestations vary with the seriousness of the injury

The general examination may reveal a pallid face, cold extremities, unconsciousness, rapid and thready pulse, low blood pressure, and other signs of serious injury

Local findings are tenderness, resistance, and muscle spasm over the side of the

EXAMINATION. The results of physical examination are negative except for the massive edema On examination soon after the appearance of the edema it is dependent, then generalized, and often associated with ascites and hydrothorax. The edematous tissue is peculiarly soft, pitting easily on pressure. The amount of edema varies inexplicably at times, and cannot be correlated with changes in the concentration of plasma proteins or the amount of protein excreted in the urine.

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When the concentration of blood urea begins to decrease and diuresis is present, caution is exercised in pursuing any immediate urge in the restoration of acid-base

they so numerous or of such character as to be confused with polycystic kidney Solitary cysts are usually unilateral. Small cysts are found in arteriosclerotic kidneys, and simple cysts may be present in kidneys that otherwise are normal These cysts result from localized obstruction, and occasionally may become very large. Hydatid and dermoid cysts are rare

Multiple cysts are occasionally confined to one part of a kidney They are compactly grouped, and the remaining tissue is normal This condition may have its origin in tubular obstruction, or it may be of congenital nature, the same as bilateral polycystic kidneys

On more detailed study, numerous areas of localized infiltration, with hyalinization of glomeruli, are present There is usually marked thickening of the smaller arteries and arteriolar walls identical in appearance with that observed in hypertensive disease This finding is a very important factor in the progress of the disease, and is associated with hypertension, which is usually present or develops as the disease progresses.

SYMPTOMS. The onset of symptoms may be very gradual, with weakness, periods of malaise, headache, nausea and vomiting In some patients renal insufficiency is manifested by rapid failure, and uremia may occur within a relatively short period of time Cerebral hemorrhage may occur in those who have hypertension which has caused no distressing symptoms prior to the stroke Complications from intercurrent disease may appear as the result of debility and anemia In some cases the only symptoms may be those caused by hypertension Congestive heart failure often occurs late

Many patients are unaware of the gradual, progressive enlargement of the kidneys which may have extended over many years prior to the onset of the first symptoms

Pain referred to the lumbar region, or to an upper, lateral abdominal region, is a common symptom The pain is usually unilateral, and is described as a dull ache, although it may become severe Occasionally one or more cysts may become of enormous size and be the cause of considerable discomfort Mechanical pressure on surrounding organs by these cysts may also be a factor in the production of pain Some patients obtain relief by lying down, others by supporting the kidneys with abdominal pads Sudden hemorrhage into a large cyst may be the cause of severe, acute pain The passage of blood clots, with ureteral obstruction, causes acute renal pain The pain may be accompanied by fever and other evidence of acute renal infection, or by ascending pyelonephritis caused by temporary urinary obstruction

Gross hematuria is present in a third of the cases It occurs at irregular intervals and frequently is brought on by violent exercise or jarring As a rule the hemorrhage is profuse and often accompanied with a clot, which may cause renal colic. The hematuria is similar to that occurring with renal neoplasm, and if but one kidney is enlarged, the two conditions may be easily confused. Microscopic evidence of blood was reported by Braasch and Schacht to have been found in the urine of 85 patients Dysuria or frequency of micturition was noted by only 15 per cent of patients

EXAMINATION On physical examination bilateral palpable tumors are present in more than one half of the patients and unilateral enlargement is present in a few Some will have no palpable enlargement of the kidneys. Although both kidneys are usually markedly increased in size, there is often a decided difference in size It is not unusual to find one kidney but little larger than normal and the other several times as large as normal Heavy muscular abdominal walls or fat may interfere with clinical recognition of renal enlargement of moderate degree. It is surprising how large a kidney may be and still escape detection on palpation As the kidneys become enlarged they frequently change their position Occasionally la[illegible]cement of one or both kidneys oc[illegible]

abdomen containing the injured kidney. A *mass may form.* The urine contains blood. There may be leukocytosis. Often there is no fever until the extravasated blood and urine begin to be absorbed or until infection becomes established

The most valuable special diagnostic means are the ordinary roentgenogram, the intravenous urogram, and occasionally, if manifestations are not severe, cystoscopic examination

Intravenous urographic examination is invaluable. It can be used successfully in patients who are unconscious and unable to tell anything about the injury and in whom it is impossible to elicit tenderness, pain, or muscle spasm The procedure not only reveals the functional capacity of the *injured kidney but also demonstrates the diffusion* of the fluid into the perirenal tissues, and also reveals the presence and function of the opposite kidney.

Renal Tumors. Renal tumors are commoner in men and children than in women *In children renal tumors are the commonest neoplasms of the upper part of the* abdomen. In adults the incidence is higher from 40 to 60 years of age than in other periods of life

Benign Renal Tumors. Adenomas, fibromas and fibrolipomas are rare. Angioma *is found still more rarely.*

The common benign renal tumor is the renal cyst There may be a single cyst, or multiple cysts that involve the entire kidney When many cysts of the kidney are present, the condition is termed polycystic disease of the kidney. The origin of these cysts is not known. They are usually small, though such a cyst may contain several liters of fluid which resembles urine Renal cysts cannot be diagnosed clinically.

A simple cyst which contains blood is known as a hemorrhagic cyst. The origin is unknown

Perirenal cysts arise from embryonic rests in the lumbar regions

Polycystic Disease. The hereditary tendency of polycystic kidney has been observed There are instances in which several members of a family, of several generations, have been afflicted with polycystic disease In 1 of Schacht's cases the condition was apparently present in representatives of four generations, in 2 cases, in three generations, and in 5 cases, in two generations. There apparently is variability in the frequency of inheritance in different families

The disease is rarely manifested before puberty The average age at which the disease becomes manifest is from 30 to 40 years, occasionally from 40 to 50 years However, some patients have no subjective evidence of disease until 50 to 70 years of age Polycystic disease affects both sexes The incidence of *congenital* polycystic kidney found at necropsy is three times as great as that diagnosed clinically (Schacht).

The cysts increase in size and multiply and the pelvis is encroached on and becomes deformed The calyces may become elongated, and broadened, while others are abbreviated or even obliterated. Polycystic kidneys are occasionally enormous; kidneys weighing 17 pounds have been observed

Coincident cystic disease of the liver occurs frequently in association with polycystic renal disease The cystic disease of the liver seldom is the cause of symptoms suggestive of hepatic disease Cysts of the liver do not usually attain great size, although occasionally they are large and it may be impossible to differentiate them from renal cysts Hepatic cysts may be observed without any accompanying renal involvement (see Diseases of the Liver, Chapter 13)

In this polycystic disease other organs besides the kidneys and liver may be involved Cystic degeneration of the ovaries, broad ligament, uterus, bladder, and epididymides may occur This fact indicates a single origin, perhaps congenital, of the condition.

Solitary cysts of the kidney probably are of acquired rather than of congenital origin. Occasionally multiple scattered solitary cysts are observed, but seldom are

The deeper situation of the left kidney is most often associated with delayed recognition of the disease. Bilateral tumors are rare

Hematuria is the first symptom; it is also the most frequent and the most important symptom. It may be painless and sudden in its appearance, and it may spontaneously disappear It may or may not recur At times it may be associated with renal colic, and the patient may pass cylindrical ureteral casts composed of blood and associated with severe pain situated in the course of the ureter. More commonly, however, there is just a dull ache in the flank. Continuous fixed pain in flank or back may be a symptom of large tumors

Weakness and loss of weight attend the progress of the disease. Fever is frequently observed with renal carcinoma In a few an unexplained fever is the only symptom. Fever is attributed to hemorrhage within the neoplasm and subsequent necrosis. Calcified deposits in the tumor visible in roentgenograms may represent the only diagnostic clue

When metastasis is present, the symptoms are referable to the organ involved This may be manifested by a spontaneous fracture of a long bone or the finding of metastatic lesions in a lung on roentgenologic examination Such lesions are found in about one third of the patients on the first examination. One half of the metastatic lesions are in the lungs, and the rest are in the bones, in the liver and in the brain.

On examination one half will have a mass in the flank or a palpable mass in the renal region by the time of the appearance of the hematuria A few patients are conscious of the mass or have had pain in the flank or along the course of the ureter. The mass is felt bimanually and is associated on palpation with deep inspiration. Coexistent prostatic hypertrophy may be found along with urinary frequency, lessened stream, urinary retention and blood clots in ureters, bladder or urethra.

The finding of variocele on the same side as the mass is frequent

Embryonal carcinosarcoma, or *Wilms's tumor* of the kidney, is one of the more frequent carcinomas of childhood It is a disease of infancy Rarely the tumor may occur in adult life, and it is then less malignant. Embryomas of this type are found equally in both sexes The tumors may be bilateral

These tumors may arise from any portion of the kidney As a rule, they grow rapidly, with large round or lobular, bosselated masses forward into the abdominal cavity.

Metastasis of embryonal carcinosarcoma is most often through the blood stream to the lungs and to the liver Lymphatic metastasis may occur to retroperitoneal and mediastinal nodes Involvement of the skeletal system is not frequent At times the tumor may grow directly through the renal capsule and involve adjacent organs

There are no signs of Wilms's tumor in its early stage Fever when present may be due to tumor necrosis or to hemorrhage within the tumor Hematuria occurs in 1 of every 10

On examination there is a mass in the abdomen or flank Pallor, weakness and loss of weight may be present with, or precede the finding of, the abdominal mass and always are present late in the disease Urinary symptoms are usually absent even late in the progress of the tumor

The diagnosis is established by pyelography and by the pressure of a mass in the side of the abdomen This mass is usually large, not tender, is rounded or lobular, and the transverse colon may be anterior to the mass if it is in the left kidney The tumor may or may not be fixed in the flank. The various other conditions presenting similar findings are carcinoma of the adrenal gland (sympathicoblastoma), chronic renal fibrosis, congenital obstructive hydronephrosis, congenital polycystic renal disease, and the retroperitoneal sarcomas of childhood

Carcinoma of the renal pelvis, arising from the specialized epithelial lining, is the same as the epithelial cancers of the ureter and the bladder. It occurs in both

On abdominal palpation, particularly if there are several distended cysts on the anterior surface of the kidney, the tumor may appear to be firm and solid

In men a *varicocele* of recent origin may occur on the left side, in association with marked enlargement of the left kidney, just as this condition occurs frequently with renal neoplasm

By the time, and often before, any symptoms of the renal disease appear, persistent *hypertension* is present In Schacht's series 61 per cent had systolic pressures of 145 mm of mercury or more In 20 per cent there was retinitis associated with retinal sclerosis In 31 per cent there was retinal sclerosis unassociated with retinitis In 6 per cent the patients had retinitis only, and without changes in the retinal vessels. In 43 per cent, examination of the ocular fundi gave negative results. It is evident, therefore, that the disease involves the entire vascular system

The specific gravity of the *urine* may be low and fixed Albumin, usually in small amounts, is present Microscopic evidence of hematuria and pyuria is often found (in Schacht's series in 180 cases, 94 per cent), in routine examinations of the urine Catheterized urine from either kidney often contains a variable number of pus cells This is apparently the result of inadequate intrapelvic drainage, caused by cysts compressing the pelvis or calyces

Normal excretion of phenolsulfonphthalein should not be regarded as excluding polycystic disease Excretion of phenolsulfonphthalein is often markedly reduced, whereas the value for blood urea is normal or only slightly elevated As the disease progresses, the concentration of blood urea increases

DIAGNOSIS The recognition of polycystic kidney is impossible without intravenous urograms or bilateral pyelograms The deformity of the renal pelvis as the result of polycystic disease is usually typical and easily recognized by the urologist It may, however, be unusual in outline and may simulate deformity seen with renal neoplasm so closely that differentiation is impossible If the renal pelves are shown to be normal, polycystic kidney can usually be excluded

The renal origin of the patient's symptoms may be first recognized in the course of routine study of renal function or urographically by intravenous pyelograms The condition may be confused with nephritis if no renal enlargement is present on palpation

After the disease is discovered, approximately half of the patients will live less than 4 years The remaining patients will live from 5 to 20 years The average age at death is 50 years.

The length of life will depend largely on the degree to which renal function is maintained The prognosis for the patient who is from 20 to 40 years of age is uncertain, since evidence of subnormal renal function usually is not marked until 40 years of age The patient observed from 40 to 60 years of age, who shows no evidence of diminished renal function, usually will live a life of normal length

Malignant Renal Tumors. The usual renal cancer is epithelial in origin, originating from the renal parenchyma or from the epithelial lining of the renal pelvis The latter, a specialized epithelium, is like the epithelium lining the ureter and the bladder, and all the tumors arising from this specialized epithelium are similar, whether from renal pelvis, ureter or bladder The tumors occurring from the renal parenchyma itself are specific tumors of that tissue

An occasional fibrosarcoma or leiomyosarcoma arises from the renal capsule These neoplasms are differentiated only by histologic study

Cahill classified renal tumors as follows (1) clear cell carcinoma, (2) granular cell carcinoma, (3) true hypernephroma (adrenal rests), (4) tumors in solitary cysts, (5) multiple papillary adenoma or carcinoma in sclerotic tubular cysts, and (6) mixed forms, among which the carcinosarcoma of infants (Wilms's tumor) is the most frequent

Parenchymal renal carcinoma occurs more frequently in men than in women in the ratio of 3 to 1. Both sexes are affected between 40 and 60 years of age

In an adult it is difficult to tell whether a stricture is congenital or acquired.

A megalo-ureter is uniformly dilated, the ureteral orifice being insufficient and allowing regurgitation of urine from the bladder If such a ureter is present and the bladder is filled with radiopaque fluid, the fluid flows up the affected ureter.

A diverticulum of the ureter is rare and may occur as a pocket which resembles a rudimentary supernumerary ureter The condition is distinguished from a cystic dilatation of the ureter.

The symptoms vary with the changes in the affected ureter and kidney, and the bladder. The patient may have ureteral pain due to the ureteral obstruction. There may be blood in the urine

Cystoscopic examination and ureteral catheterization with injection of a radiopaque medium reveal an abnormally large ureter

Ureteral Obstruction. Ureteral obstructions arise from lesions of the ureter or are due to pressure or invasion of some lesions outside the ureter. Obstructions of the ureters are thus classified as intrinsic and extrinsic, depending on their origin in reference to the ureter. They may be either strictures or obstructions of the lumen of the ureter.

Intrinsic ureteral obstructions may be classified as congenital and acquired.

Congenital Stricture. A congenital ureteral stricture is failure in development of a normal ureteral lumen. Strictures of this type are observed in the newborn and in children who have strictures without acquired urologic disease Similar strictures may be found in the presence of other malformations of the urinary tract.

The common congenital obstructing lesions are situated at or near the ureteropelvic or ureterovesical junction and at the vesical neck

Congenital obstructions at the ureteropelvic junction occur when there is too high an insertion of the ureter above the most dependent portion of the renal pelvis, or there is intrinsic narrowing of the ureteropelvic junction Obstructions at the ureteropelvic junction usually occur in young adulthood and are manifested by pain, recurrent pyelonephritis or a mass in the flank Congenital obstructions at the ureterovesical junction are bilateral

Congenital obstructive lesions at the ureterovesical junction may involve only the mucosa or may involve all the layers of the ureteral wall In the first group, the pressure of urine retained behind the small ureteral orifice causes a ballooning of the mucosa into the bladder so that ureterocele is produced Occasionally, a ureterocele may be of such proportions as to produce acute retention by obstruction of the vesical outlet In women it may extend through the urethra

Acquired Stricture. This type of stricture may be due to (1) inflammation, (2) stone, (3) trauma and (4) tumor The primary tumors of the renal pelvis and the ureter are described separately

Inflammatory lesions include infections by the colon bacillus and gram-positive cocci, and by the tubercle bacillus These inflammatory lesions of the ureter are usually part of a more general urinary infection

The common situations of nontuberculous inflammatory stricture are in the juxtavesical ureter, or the part of the ureter which passes through the wall of the bladder, and the part within the broad ligament, the pelvic brim and the ureteropelvic junction. The portion of the ureter in the vesical wall or adjacent thereto is often involved as the result of chronic cystitis, which not only infiltrates the ureteral wall but also may constrict the ureteral orifice

Stone may produce ureteral stricture by impaction and injury to the ureteral wall

Trauma, which may be inflicted during childbirth, a surgical operation, or cystoscopic procedures, may be followed by stricture

Physiologic intrinsic transitory ureteral strictures may occur during pregnancy,

sexes, slightly more frequently in men than in women, and equally in both kidneys It is more likely to occur in persons in the elderly age group than in younger persons

Renal pelvic tumors have been reported as associated with pelvic calculi and with long-standing inflammatory processes There does not seem to be any recognizable association with congenital abnormalities in the development of renal pelvic tumors

Tumors of the renal pelves arise from specialized epithelium of mesodermal origin They are classified as (1) papilloma, (2) papillary carcinoma, (3) squamous cell carcinoma and (4) undifferentiated carcinoma.

About two thirds of all tumors of the renal pelvis are papillary They may be single or multiple They are villous or wartlike growths similar to those found in the bladder and may be associated with similar tumors found in the bladder or ureters More than half of the papillary tumors of the renal pelvis are malignant

Squamous cell carcinoma in the renal pelvis is less frequent than the papillary type It occurs with irritant lesions such as infection, calculus, ureteritis cystica and leukoplakia Ulceration is common These tumors are less vascular than the papillary tumors

Infiltrating undifferentiated carcinoma occurs but is less frequent than carcinomas of other types

Tumors of the renal pelvis tend to metastasize down the ureter as well as through lymphatics to the retroperitoneal lymph nodes. From these nodes they disseminate to lungs, liver, adrenal glands and bones

The constant symptom of tumor of the renal pelvis is hematuria Pain may occur but is not constant or frequent If the bleeding is profuse there may be renal colic from a blood clot obstructing the ureter If obstruction of the pelvis occurs there may be pain in the flank

In only a small number of patients does a palpable tumor develop, a concomitant hydronephrosis is the cause of the palpable mass The mass may disappear after the passage of obstructing material General symptoms, consisting of loss of weight, strength and appetite, attend the late stages of the disease Vesical symptoms of burning, frequency and dysuria may be present if there is an associated infection

Tumor of the renal pelvis is diagnosed by cystoscopic examination and retrograde pyelograms

DISEASES OF THE URETERS

Congenital malformations of the ureters are closely associated with those of the kidneys Absence of a ureter occurs in cases of renal agenesis—solitary kidney. In such cases, cystoscopic study reveals absence of the corresponding ureteral orifice

In duplication of the ureters the malformation may be complete or incomplete. If there is complete duplication, there are two ureteral orifices each leading to its corresponding ureter and renal pelvis The corresponding double kidneys are often fused

If the ureteral duplication is incomplete, there is only one ureteral orifice and one terminal portion of the ureter At varying distances from the bladder the ureter divides, each resulting ureter pursuing an independent course to the corresponding half of a double or fused kidney

The ureteral orifice may be ectopic, prolapsed (ureterocele), stenosed, or dilated, or it may present various congenital malformations It is difficult to determine whether some of these conditions are congenital or acquired

The ureter may open outside of the bladder—in the urethra, vestibule, vagina, and, very rarely, the uterus, tubes or rectum—or it may end blindly, without any external opening. It may be an opening of a supernumerary, atrophic kidney. The commonest situations for these ectopic openings are the urethra, vestibule, and vagina, causing urinary incontinence

The diagnosis is made by localizing the stream of urine away from the usual sites for its opening in the bladder and catheterizing its opening Intravenous and retrograde urography reveal a normal bladder with one normal ureter and kidney.

Anomalies of the ureteral lumen consist of congenital stricture, valves, megaloureter, and diverticulum.

disease of the bladder may also produce complete anuria by occluding both ureters.

Incomplete Ureteral Obstruction. Ureteral lesions are much commoner in women than in men, for the female pelvis is subject to the many diseases of the adnexa, to childbirth injuries, infections incident to childbirth or abortion, and cervicitis.

The general effect of obstruction of the ureter, whether it is complete or incomplete, is urinary stasis. If obstruction is partial and the ureteral lesion remains stationary, the condition may be present for years. Renal damage is hastened if an infection or stone develops.

Partial obstruction of the ureter interferes with the expulsion of the urine, raises the intra-ureteral pressure, causes hypertrophy of the ureteral muscle, and may make ureteral peristalsis painful, owing to spasm and irritation The continuation of this pressure also produces ureteral dilatation (hydro-ureter), blunting of the calyces, hydronephrosis, and stasis of the urine Hydronephrotic kidneys may contain liters of urine; some are large enough to fill the whole abdomen. In such cases the renal parenchyma becomes a thin shell of tissue with little or no function remaining

The indirect effects of incomplete ureteral obstruction predispose to infection and formation of stones It is impossible to overcome urinary infection so long as there is poor urinary drainage The combined effect of urinary stasis and infection rapidly destroys renal function and reduces the kidney to pyonephrosis

The condition may be asymptomatic, or there may be local or general symptoms

Asymptomatic obstruction is often discovered by intravenous urography performed in a routine search for the cause of obscure symptoms. Such a discovery may explain toxic phenomena and obscure constitutional symptoms such as gastrointestinal disturbances, indigestion, gas, anorexia, headache, loss of weight, nervousness, low-grade fever, and other disturbances

The commoner types of symptoms are pain, colic, vesical symptoms, pelvic or vaginal discomfort, and dysmenorrhea These symptoms vary in intensity, without relation to the degree of obstruction

The diagnosis is made by the evidence of ureteral obstruction revealed by cystoscopic examination, ureteral catheterization, roentgenologic examination of the kidney and ureter

The diagnosis of ureteral obstruction often depends on the awareness that such a condition may be present to cause the symptoms

Ureteral Fistulas. Ureteral vaginal fistulas or ureterocutaneous fistulas may be of congenital or of acquired origin. The common form of opening of a ureter to the exterior of the body is observed in extrophia of the bladder The ureteral opening in the congenital ureterovaginal fistula is another form of ectopic ureteral opening due to prenatal influences

In the acquired type the continuity of the ureter has been interrupted and the ureter establishes a new opening into the vagina Acquired fistulas of this type usually are the result of operative injury, especially during panhysterectomy. Ureterovaginal fistula may also follow vaginal ureterotomy for stone if the distal part of the ureter is obstructed Malignant tumors may cause ureterovaginal fistula

Ureterovaginal fistulas are diagnosed by searching the vagina for the opening of the ureter Cystoscopic examination reveals the presence of but one active ureteral orifice Intravenous urogram reveals the course of the media from the kidneys down the ureters, one to the bladder and the other elsewhere

DISEASES OF THE BLADDER

When fully distended, the normal bladder contains approximately 500 ml Its capacity varies much, and it is capable of great distention without rupture In cases of retention of urine it may reach up to the umbilicus and contain 1,000 ml

when there is hypertrophy and increased rigidity and thickness of the terminal portion of the ureter

Extrinsic ureteral obstructions may be congenital or acquired

Congenital Obstruction. Fascial bands along the course of the ureter, especially near the ureteropelvic junction, occasionally cause obstruction. Supernumerary or aberrant renal blood vessels have the same effect. Ptosis of the kidney may produce kinking of the proximal portion of the ureter and thus produce ureteral obstruction. This is a very rare cause of renal colic (Dietl's crisis) and hydronephrosis

Acquired Obstruction. The causes of extrinsic ureteral obstruction include pelvic tumors, pelvic inflammatory lesions, prolapse of the uterus, surgical trauma, scars following irradiation, pregnancy, fascial bands, aberrant blood vessels, nephroptosis, or any condition which compresses, constricts, kinks or narrows the ureteral lumen so that the flow of urine is impeded

Carcinomas of the cervix, bladder or colon are frequently associated with ureteral obstruction. These tumors obstruct or compress the ureter by invading, surrounding or infiltrating the ureteral wall and compressing it.

Constriction of the ureter by tumor produces hydro-ureter, hydronephrosis, and atrophy of the kidney Infection may supervene. Infection is a factor in initiating the terminal ureteral colic, progressive renal insufficiency, and eventual uremia which are common causes of death in pelvic malignant disease.

The combined effect of the pressure of the gravid uterus, and hypertrophy of the trigonum, vesical wall, and sheath of Waldeyer with constriction of the vesical ureter often causes ureteral dilatation

Prolapse of the uterus is often accompanied by ureteral obstruction and dilatation.

Complete Ureteral Obstruction. Ureteral obstruction may be complete or incomplete It may be unilateral or bilateral It may be acute or chronic Complete ureteral obstruction is uncommon, as compared with the partial obstruction

Accidental ligation of the ureters during surgical operation and extensive pelvic malignancy are the causes of complete obstruction of both ureters.

Because of anuria bilateral operative injuries of the ureters are recognized very soon after operation Surgical treatment consisting of provision of urinary drainage is urgent because, if renal drainage is not provided, the patient dies of uremia within 2 weeks

In some unilateral ureteral ligation does not cause symptoms or fistula The kidney ceases to function and atrophies In instances in which the ureter is injured, pyelonephritis, hydro-ureter, or stricture is the eventual consequence of trauma

Cystoscopic examination reveals a normal ureter on one side The opposite ureter does not drain urine, the ureter is completely obstructed and will not allow a ureteral catheter to pass beyond the situation of the injury.

Occasionally a stone may completely obstruct one ureter Complete ureteral obstruction may be preceded by incomplete occlusion of long duration A hydronephrotic kidney which has been caused by incomplete obstruction may completely occlude a ureteropelvic junction as its weight pulls it caudad

The effect of complete unrelieved ureteral obstruction is death of the kidney If the obstruction is relieved without undue delay, under proper care and favorable circumstances the functional recovery may be complete, although such recovery usually requires months

The symptoms of bilateral acute obstruction of the ureters were discussed in connection with the description of uremia (see p. 745).

The diagnosis of complete bilateral ureteral obstruction is usually self-evident, since there is complete anuria If complete anuria occurs after a pelvic, colon or gynecologic operation, it is generally due to operative injury to both ureters It may likewise develop suddenly in persons who have bilateral renal calculi Malignant

of normal children and adults testifies how psychic tension may influence the functions of the autonomic nervous system and thus disturb its reflexes.

It is pointless to enumerate the uses the child or the adult may, more or less unconsciously, make of this debility. The physician cannot agree with solicitous parents or psychoneurotic patients concerning the alleged influence of adenoids, phimosis or a tight meatus in causing enuresis

On examination it is realized that the normal child is unable to distinguish between imperative urination and enuresis Diabetes, juvenile tabes, spina bifida, urinary tuberculosis, stone, megalo-ureter, sclerosis of the vesical neck and urethral valve are rarely found to be the cause for enuresis Urine, renal functional studies, and the sacral vertebrae (as revealed on roentgenograms) are usually within the limits of normal The intelligence quotient may be low.

Spina bifida occulta, confined to the first sacral vertebra, is extremely common *and usually does not produce enuresis The child simply and painlessly, though* to his great shame, wets the bed.

Interferences With Nervous Control of the Bladder. The bladder is supplied with autonomic (sympathetic and parasympathetic) and cerebrospinal nerves. Diseases or injury to these nerves separately or in combinations will disturb its emptying.

Section of the sympathetic nerves causes a transient disturbance in urination but this usually, in time, passes away Section of the sacral nerves causes a complete loss of voluntary micturition In time, if the bladder is otherwise healthy, the so-called isolated bladder is established Under this circumstance micturition can be incompletely performed by application of abdominal pressure as by flexion of the body There is always left from 100 to 300 ml of urine after such urination

Efferent control of the bladder is disturbed by lesions in the vicinity of the pyramidal tracts The patient is conscious of all events occurring in the bladder but he cannot initiate or control micturition This sort of disturbance of micturition occurs in tabes dorsalis, multiple (disseminated) sclerosis, syringomyelia, and early compression of the cord by a tumor The so-called cord bladder of tabes dorsalis is this type of disturbance.

In obstructions to the outflow of urine from the bladder which may occur in prostatism, sclerosis of the vesical neck and atonic sphincter with a weak detrusor muscle, overdistention causes expulsion of urine in small quantities and often a more or less constant dribbling of urine.

The first symptom of tabes dorsalis or multiple sclerosis may be dysfunction of the bladder In tabes dorsalis bladder dysfunction may be expressed by frequency of urination or impairment of renal function or cystitis, exhibiting retention due to relaxation of the vesical muscle The capacity of the bladder is increased and its mucosa is trabeculated early The neck of the bladder is open This open neck may be seen with the direct vision posterior urethroscope and shown by cystogram or urethrogram

The external sphincter alone intervenes to retain the patient's urine in the neurogenic bladder and it is usually a weakness in this rather than the level of the lesion in the cord that causes incontinence of urine.

The diagnosis of the cause of the vesical symptoms and the renal deficiency in the tabetic patient is obvious. The diagnosis is difficult when tabes and hypertrophy of the prostate occur in the same patient, or when the retention occurs in one who does not show the classic reflex changes

In the absence of prostatic hypertrophy or bar, the tabetic bladder is differentiated from the sclerosis of the vesical neck by cysto-urethrographic or urethroscopic examination Cystometry is used to differentiate the tabetic bladder from the atonic bladder

The diagnosis of disturbances in the [illegible] ... of sensory

or more, whereas if its walls are thickened, it may be contracted and hold only a few ounces. The shape of the bladder is dependent on the amount of dilatation and its attachments. The distended normal bladder is always oblong; the long axis corresponds to the long axis of the spinal column.

A distended bladder interferes with the proper execution of a pelvic examination The bladder should always be emptied before examination of the pelvis, since during this examination no definite decision is made, if the bladder is not empty, in regard to the nature of a pelvic tumor that may be present.

Congenital Malformations of the Bladder. The principal malformations of the bladder are absence, *doubling, diverticula, and exstrophy.*

Absence of the bladder and double or septate bladder are excessively rare

Diverticula of the bladder occur more frequently in men than in women and may be congenital or acquired. Those that appear in young persons, without any evidence of urethral obstruction, are called congenital, those that appear in later life, with evident urethral obstruction, are called acquired

Diverticula *may resemble double bladder, patent urachus, or trabeculations that are* the result of cystitis, obstruction and hypertrophy of the vesical musculature

Vesical diverticula may not cause symptoms unless the diverticulum has a narrow opening into the bladder, with poor drainage The symptoms when present may result from infection, calculi and tumors in the diverticula.

In exstrophy the anterior wall of the bladder and the adjacent part of the abdominal wall are *missing The result is that the posterior wall of the bladder, the trigone,* and ureteral orifices lie exposed on the abdominal wall, forming a red, sensitive, and often bleeding mass

Multiple malformations may accompany exstrophy, such as widely separated pubic bones and recti muscles. In the more profound congenital disturbances there may be prolapse of the rectum, rudimentary bicornate uterus and septate vagina There may be atresia *of the anus and the rectum may open into the* exstrophied bladder. The ureteral orifices are generally found on the lower part of the exstrophied mass.

Congenital obstructions to the vesical outlet vary widely The two common types are (1) elevation of the posterior internal sphincteric area simulating the median bar in adults and (2) contracture of the internal vesical orifice These occur in both males and females. The least common type is congenital prostatic urethral valves Whatever the immediate lesion, the syndrome of *uncomplicated obstruction* of the vesical neck is fundamentally the same as is observed in men who have prostatism (see p 431)

Disturbances in Emptying of the Bladder. When the bladder of a baby fills sufficiently to excite some mild sense of distention, it empties During the first years of life the bladder thus empties any time there is distention either day or night If a functional lack of control persists into late childhood or adolescence it is termed nocturnal enuresis or *bed wetting.*

Enuresis differs from *incontinence* of urine such as occurs after perineal prostatectomy. Enuresis differs, too, from false incontinence, the overflow of a constantly full bladder, which is seen before prostatectomy.

Imperative urination demands instant emptying of the overdistended organ of the neurotic patient or the bladder is tortured by the cramp of cystitis

Atony applies to the tired overdistended vesical muscle which may develop for example during the postpartum or the postoperative convalescences

Overflow, false incontinence, is inseparable from atony.

The functional *enuresis of childhood* is a persistence of the infantile autonomic nervous system control of the bladder without cerebral influences The child wets himself by day only under the stress of fear or great excitement unless he has a very low intelligence quotient. Normal or even intellectual adolescents and adults may rush to the toilet every few minutes before a public appearance This behavior

mucous membrane. The inflammation may be situated in any part of the bladder or over the entire organ. The bladder dilates incompletely and distention is painful. The base and the trigone are involved more than other parts. Inflammatory thickening of the mucosa may be present. This condition, called bullous edema, surrounds the urethral orifice, continues down the posterior urethra, and may be the focus of recurring cystitis. The bladder is often contracted in chronic cystitis. The infection is not especially localized around either ureteral orifice, thus distinguishing it from infections that descend from the kidney, such as tuberculosis

DIAGNOSIS The diagnosis is established tentatively by the history and the presence of pyuria. In simple acute cystitis a cystoscopic examination would be extremely painful. In general, it is well to avoid instrumentation during the acute phase of a urinary infection. When the infection becomes subacute or chronic, however, a trained urologist should see inside the bladder.

Tuberculous Cystitis. Tuberculous cystitis is described with renal tuberculosis (page 759).

Chronic Interstitial Cystitis. (*Hunner's Ulcer*). Chronic interstitial cystitis occurs preponderantly in women, often in those beyond the menopause. The disease has been observed in men It is characteristically situated in the vertex or dome of the bladder It is one of the relatively uncommon lesions of the bladder.

Urologists describe three types of lesions: a diffuse, a linear and an ulcerous type.

There is constant and often intense pain in the bladder, increased by micturition and exertion. Frequency is often intense, as evidenced by voiding every 15 minutes, both day and night.

If the patient has passed the menopause and she has chronic severe vesical symptoms of many years' duration and the urine is microscopically clear, the diagnosis is likely a chronic interstitial cystitis Cystoscopic examination establishes the diagnosis. The capacity of the bladder is often 150 to 200 ml Cultures of the vesical urine and cultures of the vesical wall are sterile.

Unusual Forms of Cystitis. When the bladder is covered by a layer of urinary salts, the disease is called *encrusted cystitis.*

In proliferative cystitis the epithelium is increased and may resemble papillary new growths A form of proliferative cystitis is *cystitis granulomatosa* The granulation tissue resembles multiple polyps or a neoplasm This form of cystitis is also designated *granular* or *polypoid* Biopsy is routine in these cases A transformation of the surface epithelium into glands is known as a *glandular cystitis* and this is similar to *cystitis cystica,* in which the wall of the bladder is covered by cystic structures Cystitis cystica is common around the internal urethra and trigone Cystic changes similar to cystitis cystica have been observed in the ureter and the renal pelvis The condition characterized by enlarged, infected lymph follicles in the wall of the bladder is known as *cystitis follicularis.*

Leukoplakia of the bladder and occasionally of the renal pelvis is characterized by thickened raised white patches Its cause is unknown A specimen for biopsy is always taken of any area of unusual or suspicious appearance to rule out malignancy.

Syphilis of the Bladder. The described lesions of syphilis of the bladder are either secondary or tertiary. The spirochete has not been found Finestone collected reports of 158 cases. Of these he accepted one report of a case in which presence of syphilis was microscopically proved, and he added reports of 2 more proved cases

Diseases of the Bladder Associated With Trauma. *Herniation of the Bladder.* The bladder is subject to three types of herniation· (1) prolapse through the urethra of the female, (2) bulge into the vagina when the pelvic floor is weakened, a cystocele, and (3) formation of part of the contents of a femoral or ingu[illegible]ia.

nerve functions and the deformity of the vertebrae revealed on physical and roentgenologic examinations

Transverse myelitis or fracture of the spinal column with complete loss of nervous function below the point of fracture or disease results in complete paralysis of the bladder and complete anesthesia of the bladder as well. The patient who has complete loss of spinal function has far greater loss of nervous control than the tabetic patient and stands the catheter far less well.

In order to prevent possible serious consequences which may follow the introduction of a catheter into the bladder of a patient who has transverse myelitis or traumatic paraplegia, it may be necessary to administer sufficient narcotic to prevent discomfort from pelvic fullness. Within 4 days the distended viscus begins to overflow Within 10 days or 2 weeks the automatic bladder will have become established and excretory pyelograms will show that the viscus contains little urine.

Urinary Retention in Women. Urinary retention in women is not common. Estimation of its relative incidence in the sexes is difficult, but urinary retention occurs many times more frequently among men than among women In most cases, if true *neurogenic dysfunction* is excluded, the cause is obscure. Such factors as pelvic operations, repeated pregnancies, infection, and urethritis seem to contribute. In some instances trabeculation of the bladder may be present, but just as often the appearance of the vesical neck is not unusual. Hyperplastic-appearing vesical necks often are reported in women who have normal vesical function and do not have urinary retention. Transurethral resection of the vesical neck, removing muscular tissue from the entire circumference, will eliminate the residual urine in most cases

Cystitis. The term cystitis is applied to several groups of diseases of the urinary bladder These are (1) acute and nonspecific cystitis, (2) tuberculous cystitis, (3) chronic interstitial cystitis and (4) other disorders which include unusual clinical types that may not be pathologically distinct or categorically classified.

A primary acute nonspecific cystitis is an uncommon disease It has somewhat different causes in women than in men. In children it is often associated with congenital malformations of the urinary and genital organs

The female bladder becomes infected from sources within the urethra such as an acute urethritis, infections in Skene's glands, urethral trauma, strictures, diverticula, caruncle and carcinoma. A cystitis may follow urethral trauma from foreign bodies introduced into the bladder or from sexual intercourse in a virgin or in a woman who has long abstained from intercourse who has passed the menopause. An acute cystitis may occur in those who have cystocele, rectocele, cancer of the cervix, uterus, bladder or infections in the pelvis which extend to involve the bladder. Pyelitis unless tuberculous in nature does not often cause cystitis The prevailing organisms found in acute cystitis are those which commonly cause urinary infections in general

Acute cystitis occurs much less frequently in men than it does in women It is in men as in women usually secondary to a urethral disorder and commonly has extended from the prostatic urethra, from the kidney as in tuberculosis of the kidney or extended from the pelvic organs A diverticulitis or a carcinoma of the colon often extends to involve the urinary bladder

Symptoms The symptoms of nonspecific cystitis are frequency, pain on voiding, pain in the suprapubic area, backache and low-grade fever. In the type called hemorrhagic cystitis the patient complains of hematuria. The constitutional symptoms are few and inconstant.

Examination. The acutely inflamed bladder should not be examined cystoscopically until the inflammation has somewhat subsided.

Acute nonspecific *cystitis* is *described* by the urologist as a hyperemia of the

vagina which begins 8 to 20 days after an extensive gynecologic operation. The incontinence is incomplete, part of the urine being passed normally with perfect control by the urethra, the urine from the injured ureter draining constantly and uncontrollably from the vagina.

In instances of vesicovaginal fistulas from various causes often the incontinence of urine is complete. The urine passes from the bladder into the vagina as soon as it leaves the ureter. The patient never voids through the urethra.

If the fistula is small there may be no incontinence while the patient is in certain positions, for instance, sitting or lying down

Urine irritates the vaginal mucosa and perineal skin. The epithelium of the vagina, labia, perineum, and buttocks soon becomes red and inflamed, and may ulcerate. It makes very little difference how small the fistulous opening is; if it leaks urine it is as annoying as a large opening. The troublesome symptom is a constant drainage of urine.

Vesicovaginal fistulas are diagnosed by examination of the vagina by means of the vaginal speculum and identifying the fistulous opening from the bladder by its drainage of urine. This finding must be verified by cystoscopic examination.

Distention of the intact bladder with methylene blue solution reveals that the bladder does not leak and that none of the methylene blue solution appears in the vagina or on the outside of the body. In some instances the methylene blue solution may drain from the bladder through a fistula to the vagina or to the outside. Bladder fistulas may form to the outside of the body after traumatic piercing, injuries of the bladder due to violence, obstruction of the ureter or urethra, tuberculosis, or malignant disease of the ureter or bladder. During the course of osteomyelitis of the pelvis or femur, sinus tracts may form which communicate with the urinary system

Tumors of the Bladder. Tumors of the bladder are often carcinomas or potentially so. Carcinoma of the bladder occurs in middle age or later and is commoner in men than in women

Urologists classify vesical tumors as papilloma, papillary carcinoma, and infiltrating carcinoma These include most of the tumors of the bladder.

There are, however, secondary types of vesical tumors which include those involving the bladder and having their origin in the cervix, endometrium, ovary, vagina, or sigmoid

Cancer of the bladder, like cancer of the lungs, has displayed an increase in incidence in recent years The cause for this increase in incidence is not known Observations by Henry, Kennaway and Kennaway in England suggest that occupational contact not only with aromatic amines but possibly also with tar, pitch and mineral oil seems to produce an increased liability to cancer of the bladder. Recent observations in experimental animals and man support the contention that carcinogenic substances excreted in the urine are responsible for the development of certain cancers in the bladder

PATHOLOGY Papillomas include the benign papilloma and the papillary carcinoma. These are the commonest types of vesical tumors Some papillomas are probably malignant from the beginning and others are always benign The malignancy or benignity of a papilloma is hard to determine. Many papillomas that are benign recur locally after removal and are easily transplanted over the whole bladder In the gross, the thickness of the pedicle, whether the tumor is pedunculated or sessile, and the presence of induration or nodular thickening of the tissue around the base are criteria of malignancy

SYMPTOMS Hematuria is the important symptom which is constant throughout the disease The situation of the tumor may cause difficulty of urination by intermittently occluding or actually infiltrating the internal urethral orifice. Blood clots too large to be voided are the commonest cause of urethral obstruction in cases

Rupture of the Bladder. Trauma of the urinary organs, particularly of the bladder, is common, largely because of injuries received by persons pursuing domiciliary tasks, by passengers in automobiles that are involved in accidents, and by persons engaged in athletics.

Any injury of the bony pelvis or blow on the abdomen may rupture or tear a full bladder. The bladder may be injured by a cystoscope or by cystoscopic procedures. The cystoscope in careless hands may perforate a bladder. A hole may be burned in the bladder by fulguration or cut out by a biopsy punch

Traumatic Rupture of the Bladder. Fracture of the pelvis or abdominal contusions may tear the bladder, producing (1) extraperitoneal rupture or (2) intraperitoneal rupture.

In rupture, either extraperitoneal or intraperitoneal, there are passage of bloody urine, or anuria, pain in the pelvic region, and shock

The history of inability to void after an accident, or the passage of small amounts of bloody urine, is important

In extraperitoneal rupture of the bladder examination reveals sensitiveness around the bladder, and occasionally there is a mass. Peritoneal irritation is present, and often a spreading peritonitis develops. The evidence of injury to the bony pelvis or the presence of tenderness in the region of the bladder or lower part of the abdomen is confirmatory. Bloody urine, obtained by catheterizing the bladder, indicates injury to the urinary tract.

The injection of a measured amount of sterile fluid into the bladder is occasionally a helpful diagnostic step. If the full amount which was injected is recovered, there is probably no gaping hole in the bladder.

The diagnosis and localization of the injury are established by local examination, catheterization, cystoscopic examination, injection of air, and roentgenograms.

Cystoscopy is the surest method of diagnosis if the patient's condition will permit the procedure.

If the bladder opens into the peritoneal cavity, injected air escapes into the abdomen. With the patient sitting upright, the pneumoperitoneum is evident on a roentgenogram, the air bubble being visible under the diaphragm.

Urinary Fistulas. There are many possible variations of these fistulas, such as urethrovesicovaginal fistula, vesico-ureterovaginal fistula, vesicopelvic-vaginal fistula, and ureterocervical-vaginal fistula (see Anorectal Diseases, Chapter 7)

Unilateral postoperative injuries of the ureter may be the direct consequence of a surgical accident such as cutting, clamping, ligating or crushing the ureter, or they may be the result of interference with the blood supply of the ureter, infection following operation, or necrosis from ligation and constriction of adjacent tissues

Postoperatively, after cystotomy, ureterotomy, pyelotomy or nephrotomy, the incision may drain urine.

Intravenous urograms reveal a normal kidney and ureter on one side, and a normal bladder On the injured side the ureter is generally dilated, the kidney hydronephrotic.

Vesicovaginal and Vesical Fistulas. The vesicovaginal is the commonest vesical fistula. There are congenital forms of vesicovaginal fistulas which usually are surgically repaired before adulthood is reached Spontaneous formation of vesicovaginal fistulas may be incident to ulceration around stones or foreign bodies which penetrate the wall of the bladder, infections which tend to ulcerate, such as ileitis or diverticulitis of the colon and tuberculosis, and radium burns. A sharp surgical knife in an untrained hand may be the cause of a urinary fistula Vesicovaginal fistula may be due to malignancy arising in the vagina, bladder or pelvic colon

Postoperative vesicovaginal fistula occurs after extensive dissections of the base of the bladder, infections, or the pressure of drains

The first indication of a vesicovaginal fistula is the presence of urine in the

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of vesical tumor Painful and frequent voiding from a secondary cystitis, and incontinence and fistula, especially vesicovaginal fistula, are often an attending complication

Secondary to ureteral obstruction and infection, the kidneys may become infected. There is pain in the course of the ureters and in the kidneys, and fever, toxemia and symptoms of renal insufficiency supervene

There is hardly any other condition which produces as many varieties of physical torture as a tumor of the bladder There are the constant symptoms of cystitis, acute pain of vesical overdistention, suprapubic pain, backache, ureteral and renal pain, sciatic pain, abdominal pain due to reflex gastrointestinal disorders, visceral pain due to metastasis, and many other types of pain and distress.

EXAMINATION Bimanual palpation of the bladder, by rectum and by vagina, is helpful, but must be done carefully to avoid breaking the tumor The important observations on physical examination are the size of the mass and its movability when the tumor is very large

DIAGNOSIS The symptoms alone are usually sufficient for making the diagnosis An objective diagnosis requires a cystoscopic examination and biopsy Biopsy of tumors of the bladder is not wholly innocuous Removal of a small piece with a fine cautery seals the tissues and is not so dangerous as some of the methods without hemostasis.

Cystographic examination is done as a part of the routine intravenous urographic study. It records a permanent picture of the capacity of the bladder and the extent of the deformity of the vesical wall and, to a large measure, the functional activity of the kidneys

There are three methods of treatment of malignant disease of the bladder: fulguration, surgical excision, and irradiation

The treatment of vesical tumors has often been unsatisfactory A survey of the subject was conducted by the American Urological Association and reported in 1939 (Orr, Carson, and Novak) This showed that the treatment of more than 26,000 malignant growths of the bladder by 267 urologists in America resulted in five-year cures in only 15 9 per cent, and that five-year cures are not always permanent

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The *blood platelets* are produced by fragmentation or segmentation of the megakaryocytes of the bone marrow.

It is evident from the foregoing that in the circulating blood there are series of formed elements: the leukocytes, the erythrocytes and the platelets The leukocytes are composed of (1) the granulocytic cells arising from the bone marrow, (2) the monocytes, which arise from the reticuloendothelial cells and (3) the lymphocytes arising from lymphoid tissue. The platelets are segmentations of the megakaryocytes of the bone marrow.

The foregoing discussion on the origin of the blood cells was made with cognizance of the fact that there is still not full agreement as to the origin of the various cells of the blood There are two theories in regard to the origin of the individual cells of the blood, namely, the monophyletic, and the polyphyletic. According to the monophyletic theory all blood cells, including the erythrocytes, arise from the lymphocytes or from the lymphoid tissues According to the polyphyletic theory the erythrocytes and the different kinds of leukocytes are derived from two, three or more parent cells (blast cells). This theory embraces all gradations of belief. There are those who think that there is a stem cell for the erythrocyte and one for each of the leukocytes

There are neounitarians who see truth in all of the theories of the origin of the blood cells and wish to combine these into one theory

These theories are of diagnostic importance in regard to the nomenclature of the cells

Nomenclature of the Blood A committee for clarification of the nomenclature of cells and diseases of the blood and blood-forming organs sponsored by the American Society of Clinical Pathologists and the American Medical Association has agreed that the choice of preferred terms shall not be based on historical priority or common usage but, in general, shall represent the simplest, clearest and most descriptive terms possible. Consistency between related terms is considered essential The committee has given detailed consideration to terminology in the erythrocytic, lymphocytic, granulocytic, monocytic, plasmacytic and thrombocytic series of cells The committee has co-ordinated its work and co-operated with representatives of *Standard Nomenclature of Disease and Operations*, of the American Medical Association, in order that proposed changes may be incorporated in that publication

So far as is possible in the present limited description of blood diseases, the *Standard Nomenclature of Disease and Operations* is followed

DISORDERS AFFECTING THE TOTAL QUANTITY OF BLOOD

Normal Values The blood has a specific gravity of 1 052 to 1 063 and viscosity of 3 5 to 5 4 These values are slightly higher in men than in women or children

The blood in healthy adults comprises about 6 to 8 per cent of the body weight Normal blood volume averages 80 to 100 ml per kilogram of body weight. This range of 20 ml. variation is accounted for in some measure by variations in height, weight, and surface area

Generally the total blood volume per unit of surface area is high in muscular and obese persons, and low in thin persons In terms of units of body weight, the blood volume is high in muscular and thin persons, low in obese persons, and greater in men than in women The plasma volume of the two sexes differs but slightly

The volume of blood in circulation in health is maintained rather constant However, it is not a static quantity There are continual additions to the circulation and losses from the circulation by the passage of water, salts and nonprotein nitrogenous products back and forth into and out of the blood stream.

Various components of blood may act independently and often do so. Water may go into or out of the blood without corresponding movements of electrolytes, proteins or other substances in it Changes in the total mass of circulating blood cells may occur unrelated to alterations in plasma volume.

Many small variations of the values for blood volumes cannot be accounted for by

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DISEASES OF THE HEMIC SYSTEM

The hemic system includes the blood, the bone marrow and the cells reticuloendothelial system which persist after birth

The blood is a fluid medium within which are suspended the cells The cells separated from their medium by centrifuging freshly drawn blood to which hepa been added The supernatant liquid thus separated is the plasma. Separation of t and the fluid medium by allowing the blood to clot and then centrifuging proc liquid, the serum

The plasma contains 90 to 92 per cent water The remaining 8 per cent is which contain 7 per cent proteins and 0 9 per cent electrolytes and the rest is co of neutral fats, glucose and many other substances

The plasma is a vehicle for carrying the blood cells but it has many and im functions not attributable to its cellular content It transports nutriments, ex products, hormones, antibodies, enzymes, and elecrolytes and aids in the maint of body temperature, to mention but a few of its functions

The plasma participates in some diseases of the hemic system as well as bei marily responsible for some of the hemorrhagic disorders, for instance, hemoph

When the blood is heparinized and the solids separated from the plasma th contains the erythrocytes, the leukocytes and the platelets These cellular element from the bone marrow, the reticuloendothelial cells and the lymphoid tissues

The *bone marrow* is composed of (1) the red cellular marrow in which bloo are formed and (2) the yellow marrow, which begins to replace the red marrow time after birth and advances until by the time of full bone growth in the early tv it has replaced the red marrow in the long bones Thenceforward, with the adv years, the yellow marrow makes but little more progress The red marrow rema the ribs, sternum, vertebral bodies, pelvis and skull, and from these foci the great of circulating elements of the blood is produced Yellow marrow does not produce

The cells of the postnatal reticuloendothelial system possess phagocytic fun These cells are identified as clasmatocytes, hemohistioblasts or macrophages by phagocytic properties and thus the ingestion of the particulate matters which co the specific supravital stains Through such staining these cells are known to be posed of two groups, namely, *fixed* cells and *wandering* cells. These designations d on whether the cells are found fixed in their usual situations in the connective reticula of the spleen, lymph nodes or bone marrow, or lining the blood sinuses marrow or liver (Kupffer's cells), or whether they are found in increased numb the site of an inflammatory reaction In the former situations they are fixed ce the latter they are wandering cells It is one function of these cells to phagocytize nants of erythrocytes and to remove discarded erythrocytes from the blood stream spleen contains many reticuloendothelial cells and it therefore is singularly conc with the function of the removal of aged erythrocytes from the blood stream.

There are blood cells which regularly arise from the reticuloendothelial syster instance, the *monocytes* of the circulating blood

Lymphoid tissue is present in all parts of the body. This tissue may occur diff as small masses, compactly, as in the simple lymph nodes, or in larger conglome as in the complex nodes and in the spleen The *lymphocytes* of the blood stream from the undifferentiated premature reticular cells of the stroma of lymphoid tiss

The *erythrocytes* and the *leukocytes* of the *granulocytic series* arise in the parts of the bone marrow. It seems that the granulocytic cells originate extravascu rather than within the capillaries as do the erythrocytes

Clinical shock in 9 of every 10 cases is produced by blood loss and thus oligemia. The fundamental feature of oligemic shock was established by Norman M. Keith.

In oligemic shock there is a reduction of blood volume so that the veins are not properly filled and consequently a decreased quantity of blood is returned to the heart. Owing to a lessened supply of blood the cardiac output is decreased, and the blood pressure thereby is lowered, inducing carotid sinus reflexes and air hunger. As compensatory mechanisms there are accelerated heart action (fast pulse), vasoconstriction (cutaneous and visceral pallor) and sympathetic overactivity with sweating.

In many discussions on shock or shocklike conditions in animals the cause of shock is attributed to excessive histamine. It has been thought that histamine-like substances liberated from crushed tissue and damaged muscles escaped into the circulation and produced capillary paralysis, loss of plasma and hemoconcentration. This traumatic toxemia theory was given first consideration as a cause of shock by those unaware of Keith's work until Blalock demonstrated that the crushed limbs of animals swelled considerably as the result of local loss of blood and plasma which was quantitatively adequate to account for the fall in blood pressure.

The Clinical Evidence of Hemorrhage. It is important to consider the rate at which hemodilution may occur in normal persons who have been subjected to blood loss Studies on the rate of hemodilution in human volunteers made by Wallace and Sharpey-Schafer showed that, after a loss of 20 to 25 per cent of the blood volume, full hemodilution was not achieved until 32 hours, on the average, had elapsed The hemoglobin reading immediately after an injury may thus be a poor index of the severity of the bleeding

The best evidence pointing to hemorrhage as the most important factor in shock includes the history of the amount of blood lost, the physical examination—for example, gross swelling of the soft tissues in a wounded part can accommodate considerable quantities of blood; and the clinical course. The response to early and adequate transfusion makes it evident that patients in very profound shock may recover completely when the blood volume is restored, provided further hemorrhage can be arrested.

Circulatory collapse due to plasma loss occurs in burns and crushing injuries As a result of tissue trauma in burns and crushing injuries the permeability of the capillaries is altered and a fluid closely resembling plasma passes out into the tissues. The more important sequela of this type of trauma is renal failure, the syndrome which is termed the crush syndrome

In a few patients who have shock from severe injuries the blood pressure on first examination may be found to be raised These patients are pale, and the radial pulse may be of small volume. These patients often subsequently manifest the commoner signs of oligemic collapse with or without evidence of intracranial hypertension

Blood losses up to a liter are well tolerated by normal persons As long as such persons remain recumbent the signs of shock are not clinically obvious, apart from slight acceleration of the pulse and reduction of blood pressure by about 10 mm of mercury The blood pressure seems to be maintained by an increased peripheral resistance During this stage of hemorrhage there is a considerable reduction of the volume of blood in the systemic venous system and also a reduction of the volume of the pulmonary vascular system

Blood donors may faint during the withdrawal of 500 ml of blood. When such a collapse occurs, the fall of blood pressure is accompanied by a slowing of the heart rate. During the faint the right auricular pressure rises and the cardiac output is slightly increased Vasovagal collapse seems, therefore, to be due to a sudden loss of peripheral resistance (see Carotid Sinus, Chapter 5). The condition usually subsides spontaneously in the recumbent position

sex, age, habitus, muscularity or adiposity, activity, state of hydration, and condition of the heart and blood vessels. It is these variations which have limited the use of the values for blood volumes in diagnosis.

All but excessive additions or losses of blood only temporarily affect the blood volume. If a transfusion of blood is given to a normal person, water and electrolytes escape, the extra erythrocytes are forced out of circulation, and within 2 or 3 hours the blood volume returns to normal.

A transfusion of 500 ml. of blood in an adult may increase the erythrocyte count and the hemoglobin as much as 8 to 10 per cent within one day but no more thereafter. The erythrocyte count may be increased by 1,000,000 cells per cubic millimeter if 15 ml. of blood per kilogram of body weight is administered. Transfused leukocytes are almost immediately removed from the circulating blood Diuresis and a visible diminution of edema will follow a blood transfusion if the patient has been edematous and has normal concentration of serum proteins. A fever, if due to the anemia, will subside within one day.

Intravenous infusions of dextrose or saline solutions have only a slight, transient effect on the blood volume, since the water leaves the vascular system almost as fast as it goes in Plasma, albumin, amino acids and acacia have a little more prolonged effect.

It appears that the blood volume, which in health is fixed and regulated at a constant optimal level for the individual, may be changed and maintained at a different level in disease, and attempts to make a quick change in the new abnormal blood volume are resisted by the body. Severe chronic hemorrhage with unrelieved oligemia results in fixation of blood volume at an abnormally low level This condition has been termed chronic shock

Acute losses of blood are followed by immediate entrance of extravascular water into the blood stream This is followed more slowly by the entrance of protein and cells If the blood loss has been large, these compensatory mechanisms are inadequate. In such instances restoration of blood volume depends on transfusions or on the slow natural process of blood regeneration.

Reductions in blood volume are compensated for by. (1) tachycardia and more forceful heart beats; (2) polypnea which aids return of blood to the heart; (3) vasomotor effects which shift blood to the vital centers; (4) increase of plasma by an influx of fluid from the tissues; (5) mobilization of protein and surplus erythrocytes and (6) prevention of anoxia by a rising coefficient of oxygen utilization Severe hemorrhage may cause the blood volume to fall so low that the body is no longer able to adjust to the deficiency.

A *blood volume increased* to an abnormally large amount often is beneficial when it develops slowly as a compensatory response to polycythemia vera, congestive heart failure or free arteriovenous communication A blood volume increased to an abnormally large amount, produced by rapid transfusion of large quantities of blood, may do harm by embarrassing the heart or by producing such secondary effects as hemorrhage, pulmonary edema or renal failure

Changes in blood volume in disease are rarely of diagnostic aid except in shock and perhaps in polycythemia vera

Shock. The term shock is employed to describe many and diverse states, conditions or actions Here the term is employed to designate an acute peripheral circulatory failure due to loss of circulating fluid or derangement of circulatory control brought about by injury.

Any attempt to produce a clinical classification of shock can be only provisional Blalock's classification into hematogenic, cardiogenic, neurogenic and vasogenic forms often is difficult to apply in clinical practice owing to the lack of accurate knowledge of the complex interrelations of the contributing factors in any given case. McMichael's classification of shock includes such varied causes of shock as hemorrhage, vasovagal syncope, pulmonary embolism, bacterial toxemia, diabetic coma and the crises of Addison's disease, it too is difficult of application.

volume, the blood pressure level is the most valuable sign for early diagnosis of clinical traumatic shock in which hemoconcentration does not occur

To summarize, it must be stated that for practical purposes the recognition of shock will have to be based on the presence of a combination of the commonest manifestations and features, as constituting the most adequate means of detection of the presence of shock. The objectivity of blood pressure determinations increases the significance of very low blood pressure readings in the state of shock. In practice it is inevitable that in a certain proportion of cases peripheral collapse will progress unrecognized until a stage of irreversible circulatory deficiency has developed

Reactions from the Transfusion of Blood. A transfusion of blood may be followed by a febrile reaction The fever often is not accompanied by other symptoms. In some instances the temperature may reach 104 to 105 F (40 to 40 5 C) but this lasts only a few hours A chill and subsequent fever may follow within an hour after the transfusion, or may be delayed for 24 hours. These reactions may be due to small thrombi in the transfused blood In some instances there may be excessive alkali or acid in the diluting fluids. The rubber tubing has been held responsible for reactions because it contained soluble toxic substances, or it was not sufficiently cleansed and thus contained bacterial proteins Excessive quantities of blood or parenteral fluids given in the presence of advanced myocardial weakness may be followed by sharp coughs, precordial pain, back pain, dyspnea and cyanosis which indicate right-sided cardiac failure Such a reaction may progress to pulmonary edema and terminate fatally

Allergic reactions characterized by urticaria, swelling, swollen throat and joints, lymph node enlargement, and fever may follow a blood transfusion These may not be related to the volume of blood given A leukocytosis follows transfusions.

Incompatible blood may produce symptoms before much blood has been introduced, and if the transfusion is stopped, often no serious injury results The symptoms are precordial oppression and pain, restlessness, anxiety, flushing of the face, b[illegible] d respiratory rates [illegible] weak pulse, a chill, [illegible] occasionally delirium without evidence of shock Hemoglobinemia, hemoglobinuria, hemorrhagic tendencies, jaundice, oliguria or even anuria may follow. Anuria and uremia may be followed by diuresis and recovery The ultimate prognosis in regard to the kidneys in a given case of hemolytic reaction to transfusion is determined by the degree of tubular damage or the severity of the lower nephron nephrosis.

If the patient is already in shock and incompatible blood is given, immediate symptoms may not be detectable, but a delayed fatal reaction may ensue within a week.

There are substances in both the erythrocytes and the serum of the blood which may cause transfusion reactions

The Blood Groups. The serum of certain persons when mixed with a suspension of red cells from certain other persons causes agglutination of the cells. This phenomenon is attributable to the presence of substances known as iso-agglutinins. Human serum [illegible]

[illegible] whenever an agglutinin and its corresponding receptor are present.

A characteristic of the erythrocytes is the possession of receptors and this factor determines the blood group. This trait is inherited as a dominant mendelian

It seems that when shock is profound (systolic blood pressure lowered to 60 mm of mercury or less), the circulating blood volume has often been reduced to 2 liters or less This opinion is substantiated by the quantities of blood or plasma required to bring the blood pressure back to normal However, chronic reductions of blood volume attained slowly as in a severe anemia are common without vascular hypotension

In severe shock the pulse is rapid, but it is seldom more than 120 per minute, while at other times it is slow (80 per minute) in the presence of a low blood pressure.

Chronic Reduction of Blood Volume. The chronically ill patient with loss of weight and debilitation is more susceptible to shock, less able to tolerate a minimum of hemorrhage, is intolerant of isotonic sodium chloride solution and frequently displays fluid and salt retention after such infusions The weight depletion and the other reactions are not associated with an actual reduction of the potential vascular bed but often are associated with a reduction of plasma proteins and total blood volume For these reasons it has been found that blood volume and the total electrolyte deficits in depleted patients should be calculated on the basis of a standard for the usual weight prior to the illness. If these calculations are made and the electrolytes and plasma proteins are replaced, these patients are less likely to suffer shock after small hemorrhages at the time of surgical operation

Criteria For Recognition of Shock. The common factor in the production of shock is a discrepancy between the effective circulating blood volume and the actual volume capacity of the vascular bed. This discrepancy is primarily responsible for the clinical symptomatology consisting of a low body temperature, feeble and rapid pulse, cold skin, exhaustion and decreased arterial pressure. When these manifestations are present, shock may be profound and therapy may be ineffective. It is therefore desirable to have criteria which will express the earliest, asymptomatic phase of the disparity between blood volume and vascular bed.

The basic disturbance in all types of shock is a *reduced blood volume.* Estimation of the blood volume can be regarded as the most logical index of impending shock The determination of blood volume is feasible in practice by the use of Evans blue dye However, this method would not be adequate for following the progress of shock since estimations cannot be repeated at frequent intervals.

Hemoconcentration may be used for the recognition of shock According to Moon it constitutes the earliest detectable manifestation of shock as well as the most accurate index of its severity Mainly on the basis that absence of hemoconcentration expresses normal capillary permeability, Moon contends that hemorrhage should be differentiated from shock, since hemorrhage is accompanied by hemodilution and only terminally may be associated with hemoconcentration. In contrast to this concept, Blalock has shown that an irreversible typical syndrome of shock with pathologic signs of increased capillary permeability, which is as a rule associated with hemoconcentration, may be elicited by slow removal of blood. Davis also observed identical pathologic features in protracted hemorrhage and in traumatic shock The differentiation between shock and hemorrhage has not been generally made. Harkins summarizes this point of view, stating that a differentiation between hemorrhage and other types of shock would not have any diagnostic, prognostic or therapeutic value In patients often both whole blood and plasma are lost Hence hemoconcentration is not a regular feature and, except in cases of burns, cannot be relied on as an accurate sign for recognition of early clinical shock.

Many clinicians believe, and perhaps rightly so, that the detection of a low or falling arterial pressure constitutes the most reliable early clinical feature of shock The value of blood pressure readings has been emphasized by Evans and his associates, who concluded that, as compared with hemoconcentration and blood

kept at icebox temperature, agglutination may occur (cold agglutination). The clumps break up as soon as the mixtures are warmed Such serum will similarly clump any red cells added to it. This reaction is not specific but has been used empirically in the diagnosis of atypical pneumonia.

Acute hemolytic anemia has been recorded in patients whose blood contained cold agglutinins in high titer. Some have attributed this to intravascular agglutination resulting from chilling of the extremities

Despite all known precautions in obtaining and preparing blood for transfusions, there remain indeterminate individual differences in human blood in addition to those represented by known factors Unfortunately these individual differences cannot always be detected in all instances and transfusion reactions may ensue

Infections From Blood Transfusions. Homologous serum jaundice, infectious hepatitis, malaria and syphilis have been acquired from blood transfusions

REACTIONS TO ADMINISTRATION OF LIVER EXTRACTS

Reactions to liver extract occur in about 1 of every 10 of those who receive it Intramuscular injection of liver may cause local pain, tenderness, fever, and an area of induration at the site of injection.

Reactions to parenteral administration of liver may be observed when preparations of whole (crude) liver are administered These reactions are of two types, immediate and delayed

The symptoms of the immediate reactions from the injection of liver extract commence in from 5 to 30 minutes after injection and consist of nausea, weakness, faintness, and palpitation There may be generalized itching, tingling and flushing of the skin Choking sensations or actual choking and angioneurotic edema, substernal pain, pain in the back and collapse are rare

The symptoms of the delayed reactions are not severe These reactions commence from one day to one week after liver extract is given The manifestations often are itching and flushing of the skin with or without urticaria Chills and fevers, vomiting, and discharges from the nose and eyes are common

Once reactions have appeared, they usually increase in severity with subsequent injections Mild reactions may be controlled by injecting smaller doses, and the immediate symptoms are relieved by injection of 0 5 ml of epinephrine solution (1:1,000)

SUSPENSION STABILITY OF THE BLOOD—THE SEDIMENTATION TEST

Variations in Disease. The erythrocyte sedimentation reaction is a nonspecific reaction which is said to give information concerning the morbid processes within the body The reaction may be accelerated when the temperature, pulse and leukocyte count are normal, particularly in chronic disorders and in localized inflammatory diseases It likewise may not be accelerated when all the foregoing data are abnormal When broadly and liberally interpreted, the sedimentation rate is increased in acute general infections In acute catarrhal inflammation the rate tends to be normal In localized acute suppurations, such as pelvic inflammatory disease, there is often an acceleration In chronic localized infections the rate varies with the extent and nature of the infection The blood sedimentation tends to be accelerated in the presence of malignant tumor which has begun to produce failure of health

The sedimentation reaction is a worthless test for the detection of the presence of a specific occult disease, for so many times it is accelerated in those who are in good health and who remain so for months and years after having had an accelerated sedimentation rate A single accelerated sedimentation is never more than an interesting observation unless it is very high It is the trend toward an increase or a decrease in acceleration of sedimentation of the erythrocytes which is of the greatest clinical value.

character The group characters are often incompletely developed at birth, especially the agglutinins, but become evident after 3 to 12 months. After these have once developed, the group never changes, although the agglutinating activity of the serum may vary or even disappear. Since possession of receptors by the red cells is the factor which determines the blood group, it is preferable to designate the groups by symbols which indicate their receptor content, rather than by arbitrarily chosen numerals The four groups therefore are termed A, B, AB, and O (no receptors)

The Agglutinogens A_1 and A_2. Clear-cut subdivisions of the major blood groups have been demonstrated only in groups A and AB. If the agglutinative activity of properly selected group B or group O sera are titrated with cells from many group A individuals, the latter fall sharply into two subgroups. One subgroup possesses cells which are agglutinable in relatively weak dilutions of serum, whereas the cells of the other are agglutinated only in relatively high concentrations The titer for cells of the first subgroup may be four to eight times that for those of the second subgroup. Landsteiner and associates on the basis of absorption tests and other procedures attribute this and other differences between the subgroups to the possession of different agglutinogens in the cells, they designated the readily agglutinable subgroup as A_1, the other as A_2. Subgroup A_1 is about four to five times as numerous as A_2 Serum from group O and group B usually contains two agglutinins active on A cells, one, known as anti-A or α, agglutinates both A_1 and A_2 cells, about equally, the other, anti-A_1 or α_1, agglutinates only A_1 cells

The Rh Factor In rare instances patients who have received repeated transfusions of blood from donors of the homologous major blood group eventually exhibit severe hemolytic reactions although previous transfusions even from the same donor had caused no reaction It has been shown that these reactions in most cases are due to the development in the recipient of antibodies for an agglutinogen in the cells of the donor which is different from A_1, A_2, B, M, and N To this agglutinogen the term Rh is given because the corresponding anti-Rh agglutinin is identical with one which can be produced in rabbits by injections of blood from rhesus monkeys By use of agglutinating sera from such patients or from immunized animals, the Rh agglutinable factor can be demonstrated in about 85 per cent of (white) persons tested In the 15 per cent who were Rh-negative, normally no anti-Rh agglutinin is demonstrable. It may appear (only) after immunization, either as a result of repeated transfusions of Rh-positive blood, or as a result of pregnancy when the fetus is Rh-positive Immunization occurs, however, in only about 2 to 4 per cent of the cases in which it might be expected.

In a woman so sensitized a first transfusion of Rh-positive blood may cause a hemolytic transfusion reaction Antibodies from the mother may also gain access to the fetal circulation and cause erythroblastosis For such sensitized patients it is imperative to have Rh-negative donors

Blood sera taken from different sensitized individuals may differ qualitatively in their agglutinative action on various Rh-positive cells Three specific types of agglutinating sera have been recognized (1) the standard anti-Rh serum (anti-Rh_0) which agglutinates the red cells of 85 per cent of the individuals tested, (2) a type (anti-Rh') which agglutinates the cells of 70 per cent, and (3) a third (anti-Rh") which agglutinates the cells of only 30 per cent Between 1 and 2 per cent of individuals are Rh-positive, but this is not detected by use of the first type of serum. Certain sera may contain two agglutinins, for example, anti-Rh_0 and anti-Rh', or anti-Rh_0 and anti-Rh"

Minor (Cold) Agglutinins In certain cases the serum of one individual may agglutinate the cells of another belonging to the same blood group, or to group O, even if the action of anti-Rh agglutinins is excluded, provided the mixtures are kept at icebox temperature. These reactions are dependent upon the interaction of several different agglutinin-receptor pairs, only one pair, P_p has been extensively studied These agglutinins are independent of the four blood groups, A, B, AB, and O. They are weak and occur only in high concentrations of serum and rarely cause transfusion reactions When transfusion reactions occur, they are due to errors in group determinations

In rare instances when mixtures of serum and cells from the same individual are

from the megakaryocytes, the multinucleated giant cells of the bone marrow, as pinched-off fragments of the cytoplasm of these cells. Howell (1937) demonstrated that in cats they are formed from megakaryocytes lying in the pulmonary capillaries rather than in the bone marrow. In pathologic conditions, particularly in chronic myelogenous leukemia, occasionally in Hodgkin's disease and pernicious anemia, large masses of cytoplasm may be found in blood films.

In these conditions *megakaryocyte nuclei* occasionally are found in the blood The typical, large lobate nuclei seen in marrow films cannot pass through the pulmonary capillaries, but small nuclei or nuclear fragments may get through. They are two to four times the diameter of an erythrocyte or larger, and round, oval, or irregular in shape

The blood platelets are indispensable for normal blood coagulation Their life is brief, about 3 or 4 days. They are thought to be removed by the spleen and other reticuloendothelial tissues The normal number (150,000 to 250,000 per cubic millimeter of blood) varies with the method used to count them.

Platelets are increased in most conditions associated with active cell formation in the marrow. Among these conditions are (1) many acute infections, (2) after hemorrhage, (3) chronic myelogenous leukemia, (4) polycythemia and (5) Hodgkin's disease

Platelets are diminished in (1) idiopathic purpura haemorrhagica, (2) pernicious anemia, (3) aplastic anemias, (4) acute leukemias (the "primary" thrombopenias), (5) some severe infections, (6) acute or chronic poisoning with benzol, radium, arsphenamine, gold salts, phenylethylhydantoin (mirvanol), sedormid (allyl-isopropyl-acetyl-carbamide), barbiturates (rarely) and other agents and (7) after excessive radiation (secondary thrombopenias)

Coagulation time (Lee and White) is from 5 to 8 minutes The *bleeding time* is usually stated to be 1 to 3 minutes depending on the method employed

The Purpuras. The purpuras are manifested by spontaneous hemorrhage in the skin, mucous membranes, and internal organs

Purpura Haemorrhagica (*Werlhof's Disease*) Purpura haemorrhagica is called also essential, primary, thrombocytopenic or idiopathic purpura These purpuras are due to a decrease or to an absence of blood platelets

The cause of the disease is unknown Purpura haemorrhagica is principally a disease of children and young adults It is uncommon in the aged The disease has been present at birth in full term and premature infants and is known to have been present in both the infant and the mother

A well-pronounced individual familial and racial tendency to the disease is prone to be manifested in early life Members of the white race are more likely to be affected than those of other races There is, however, no clearly defined, sex-linked, inherited trait The disease is commoner in girls and young women than in boys and men. It is uncommon in Negroes

There is an inability of the blood to coagulate and control capillary leakage. The defect in coagulation is apparently due to a decrease of platelets, a thrombopenia

The consensus regarding the *cause of the thrombopenia* is that it is a disease of the bone marrow in which one or all of the following abnormalities are extant a decreased formation of blood platelets or increased destruction of platelets, or increased requirements for them

Symptoms The symptoms usually appear suddenly in a person who has a history of having bruised easily for some time or for a long time The first symptom may be spontaneous epistaxis, especially after acute respiratory infection or heavy cigarette smoking The cutaneous lesions are manifested by a few scattered petechiae or successions of ecchymoses into or beneath the skin These appear most frequently on the extremities, neck and thorax but may appear anywhere They may be extensive and cover a large part of the body. Unless epistaxis and bleeding of the gums have occurred, the patient will not complain of oral lesions.

Excessive bleeding may follow surgical operations such as dental extraction and tonsillectomy, or more frequently may occur after cuts and slight injuries. Subcon-

SOME POPULAR CONCEPTIONS OF THE BLOOD

There is the popular conception that relationships by descent from a common ancestor have been determined by the character of the blood. The terms pure blood, good blood, full blood, and half blood by the same token reflect the implication that blood is the part of an individual which determines the social and the biologic qualities of that individual National and racial differences too are qualified by such terms as German blood, English blood, Negro blood These popular conceptions have no scientific foundations Blood in no way influences the transmission of hereditary characters. The idea that "blood is thicker than water," indicating a blood tie between members of a family or individuals, is completely false. It is now clear that the only blood tie between human beings is the fact that they are members of the species *Homo sapiens*. The hemic traits, like all other traits, are determined by the presence or absence of certain genes in combination with one another The blood has no causative influence on the combination of genes It is subject to the influence of gene combinations the same as all other tissues. Thus there are inherited normalities and abnormalities of the various constituents of the blood the same as there are of the other tissues of the body.

COAGULATION OF BLOOD AND HEMORRHAGIC DISORDERS

In this section are included those hemorrhagic disorders of the blood which are due to faulty coagulation or to the increased capillary permeability

The active ingredients necessary for the formation of a blood clot are derived from (1) the blood plasma, (2) the blood platelets and (3) the aqueous tissue extracts

The *blood plasma* contains prothrombin, calcium, thromboplastin, fibrinogen and heparin The prothrombin is formed in the liver, and on coagulation of blood is converted to thrombin by the action of thromboplastin with calcium acting as a catalyst. Thromboplastin is abundant in the blood platelets as well as in the plasma and tissue extracts The thromboplastic activity of tissue extracts is derived in part from or accounted for by the presence of cephalin. Just how thromboplastin converts prothrombin to thrombin is not known

Fibrinogen present in the plasma is converted to fibrin by the action of thrombin The fibrin is the basis of the clot. A blood clot without platelets remains soft, with platelets it becomes firm and retracts

The presence of heparin seems to prevent the blood from coagulating within the circulatory system.

Aberrations in the presence and functions of the forementioned substances in the blood are the basic causes for failures of the blood to clot

The failure to form the proper blood clot is the cause for many hemorrhagic disorders In some hemorrhagic disorders the lack of a particular substance, such as prothrombin in liver disease, can be determined In many others the actual origin of the hemorrhagic disease is not wholly determinable. Other causes of hemorrhagic disorders are aberrations in the erythrocytes and infections of the erythrocytes as in malaria and *Bartonella bacilliformis*

The etiology, the manifestations and the classification of the diseases affecting the blood-clotting constituents of the blood may be confusing In an attempt to clarify somewhat the confusion, Fowler has separated these so-called hemorrhagic states into three types. (1) There is a failure of the clot to retract and become firm owing to a lack of platelets (2) In some instances the elements of the blood may be normal, and there is present weakness or an increased permeability of the capillary walls. It seems too that in some instances there may be a combination of these features in the same patient (3) In some there is a failure of the clot to form owing to a deficiency of one or more of the substances concerned in normal clot formation.

The *blood platelets*, or *thrombocytes*, are round or oval bodies, usually 2 to 3 microns in diameter, although they vary greatly in size and shape. In films they show a marked tendency to form clumps They contain no nuclei They are believed to arise

for recovery after successful splenectomy are better than 1 out of 2. Hemorrhage into various parts of the nervous system is the commonest serious complication. However, recovery has been observed after intracranial hemorrhage.

Symptomatic Purpura. The symptomatic purpuras are associated with a diagnosable disease or a poison. Recovery from the causative disease or the poison ameliorates the purpura. These purpuras are due to capillary fragility

In any *infection* which causes a high fever, such as septicemias, typhoid fever, subacute bacterial endocarditis, miliary tuberculosis, rickettsial fevers, smallpox, vaccinia, scarlet fever, and measles, purpura often occurs

Physical agents, chemical, vegetable, and *animal products,* of diverse origins cause purpura and thrombopenia without affecting the erythrocytes or leukocytes except for the losses incurred from hemorrhage. Thrombopenia may develop and purpura may be associated with burns, sunburn and sunstroke

The *organic arsenicals,* some hypnotics, and sulfonamides may induce purpura The development of purpura in an adult should arouse suspicion of a drug as the etiologic agent

Many *vegetable foods* may cause purpura Of the vegetable cosmetics, orris root may be mentioned as being of etiologic importance.

The important *animal products* as causative agents are various immune sera and the venoms from snakes and insects

Purpura, thrombopenia, prolonged bleeding time, nonretractility of the clot and positive results of the tourniquet test are manifestations of a purpura originating in the hematopoietic system In the acute leukemias immature leukocytes are present In the acute, subacute and chronic forms of this disease there are fever, a cachectic state, ulceration in the mouth, glandular and sometimes hepatic enlargement. In the aplastic anemias thrombopenic purpura is accompanied by leukopenia, relative lymphocytosis and few or no signs of erythrocyte regeneration Myelophthisic anemia may be accompanied by purpura Extensive metastasis may be present for some time before roentgenograms of the bones will reveal the presence of the causative lesions.

In Banti's syndrome, Gaucher's disease, Felty's syndrome and hemolytic jaundice the great size of the spleen, as well as other objective findings, is often sufficient to distinguish these conditions from purpura haemorrhagica

The diagnosis of the symptomatic or secondary purpuras can be made only when there is present a well-defined capillary weakness manifested by positive tourniquet reactions There is no well-defined abnormality of the blood These same diagnostic criteria apply in purpura simplex, purpura senilis, purpura cachetica, orthostatic purpura, allergic purpura and vitamin deficiency purpura

In thrombocytopenia the platelets are reduced, the bleeding time prolonged, the coagulation time slightly delayed, clot is nonretractile, the tourniquet reaction uncertain, and there may be changes in the leukocytes

Allergic Purpura. Allergic purpura is known also as Schonlein-Henoch purpura, peliosis rheumatica, anaphylactoid purpura and hemorrhagic capillary toxicosis

Nonthrombopenic purpuras occur in association with symptoms of allergy, for instance, edema, erythema and urticaria The purpuras which are classified as of allergic origin are Henoch's purpura, Schonlein's purpura and the purpura associated with erythema simplex, erythema multiforme, erythema bullosum, erythema vesiculosum, erythema nodosum, and urticaria pigmentosa (see Chapter 18).

The predisposition for allergic purpura is the inheritance of the allergic state. The exciting cause may be bacteria or bacterial products (vaccine) or an article of food. In some instances a hypersensitivity to cold or to heat or to sunshine may be the cause for purpura

A mild edema may be present on the face, in the hands or feet, or about the knees and elbows, and this may be the only complaint An allergic purpura may

junctival or retinal hemorrhage or hemorrhage into the tongue may be present Hemorrhagic bullae and hematomas frequently are complained of in severe instances of the disease.

Bleeding from the urinary and genital organs is frequent. Uterine bleeding may be often expressed by profuseness and duration of the menstrual period and may be the only symptom of the disease. Purpura haemorrhagica may commence at puberty or even before, and may then be manifested by vaginal bleeding or menorrhagia. Hematuria is a common symptom which may originate in any part of the urinary tract from the renal pelvis downward.

Melena or, less frequently, hematemesis indicates bleeding in the upper part of the gastrointestinal tract Rectal bleeding is less common than bleeding from the upper part of the alimentary tract. Hemorrhage into solid viscera does not occur in this disorder

Intracranial hemorrhages are often multiple and vary in size from petechiae to large extravasations of blood producing in some cases pachymeningitis or hemorrhagic encephalitis Intracranial hypertension is not produced by this disorder. The brain, the spinal cord, and the cerebrospinal meninges are all equally affected

Examination. *The patient's skin may be normal in appearance with an occasional petechia or areas or splotches of ecchymosis, or it may be covered with* petechiae and ecchymoses The lesions are deep red, purple, brown or yellow, depending on their age. In a third of the cases the spleen is palpable but not greatly enlarged The physical findings depend on the extent and site of the bleeding. Rarely is there shock If there be intracranial bleeding, the most frequent signs are those of hemiplegia or meningitis

The application of a tourniquet or a blood pressure cuff to the arm is followed by the appearance of numerous petechiae (a positive reaction to the tourniquet test)

The blood *platelets* are greatly decreased in number, and they vary in size; giant forms, minute platelets and deeply stained ones are reported The platelets may be absent There is some correlation between the platelet count and the severity of bleeding In acute exacerbations of the disease bleeding usually does not occur *unless the platelets are fewer than 50,000 per cubic millimeter* of blood. In chronic disease the platelet count may remain less than this without hemorrhages

The bleeding time is prolonged and a failure of the blood clot to retract is confirmatory evidence of the thrombopenia. The coagulation time of the blood is within the normal limits

The anemia in acute purpura is normocytic and proportional to the extent of blood loss Immediately after a severe hemorrhage, there may be macrocytic anemia. When the bleeding has been severe and long continued, the anemia may *become* hypochromic and microcytic in type.

The leukocyte counts in acute purpuras reveal normal numbers In chronic purpuras there may be a relative lymphocytosis

Diagnosis. The platelet count is reduced, the bleeding time is prolonged, the clot is nonretractile, and the coagulation time is essentially normal Anemia may be present; if so, it is proportional to the blood loss There is a positive tourniquet reaction There may be morphologic platelet changes. The diagnosis *of purpura* haemorrhagica is made after toxic causes for thrombopenia are known to be absent

In the differential diagnosis the pre [illegible] and changes in structure and size of the lymphocytes is [illegible] of purpura haemorrhagica The nonthrombopeni[illegible] om purpura haemorrhagica by the family history and by manifestations of allergy.

In all proved instances *of acute purpura haemorrhagica, even* after many relapses, recovery usually takes place. However, there are chronic instances of the disease from which the chances for recovery are fewer than 1 out of 3 The chances

which there were spontaneous ecchymoses in 88 members, is similar to the form described by Giffen.

The diagnostic criteria for purpura simplex are the presence of mild purpuric skin manifestations unassociated with definite abnormalities in the blood The tourniquet test is positive. Rheumatoid arthritis and rheumatic fever are frequently associated

Pseudohemophilia (Hereditary Hemorrhagic Thrombasthenia, Thrombasthenia Purpura). Pseudohemophilia belongs to the group of hereditary hemorrhagic diatheses. It is a hereditary disease with no predilection for sex. The disease has been considered to be due to a *congenital capillary dysplasia* Others have considered the condition to be due to thrombasthenia, the platelets, however, are normal. The disease may begin in infancy or at any time thereafter.

The clinical symptoms are similar to those of hemophilia There are recurrent nosebleed, hemoptysis, hematemesis, vaginal bleeding, hematuria and hemarthrosis. The bleeding may follow slight trauma and may be mild or severe and in some instances fatal

On examination there often is neither anemia nor splenomegaly The blood cells and platelets are normal The bleeding time is prolonged but the coagulation time is normal. Thus the changes in the bleeding and coagulation time are the opposite from those present in hemophilia The tourniquet test is positive.

In diagnosis, the genealogic history signifies that the bleeding tendency is transmitted by both sexes The bleeding time is prolonged, but there are normal numbers of platelets and coagulation time is normal A family history of epistaxis may be accepted as evidence of the hereditary nature of the disorder.

Hemophilia. In hemophilia there is a permanent inborn defect which inhibits blood coagulation This defect is hereditary in origin and is sex-linked It is a recessive mendelian trait.

The disease is limited to the male but is transmitted from the male through an unaffected daughter to her son. The sons of an affected man cannot transmit the defect to any of their descendants Only the daughters are capable of transmitting the trait Females never manifest the disease

Long inheritance through females, with the males being insufficiently affected to manifest the disease, is an acceptable explanation of the occurrence of *sporadic cases* of hemophilia.

It has been well demonstrated that there is no lack of fibrinogen, no calcium deficiency, no reduction in number of platelets The defect seems to be present in the plasma Plasma thromboplastin is absent or reduced in hemophilic plasma. The globulin fraction of the plasma proteins contains the so-called antihemophilic globulin or the globulin substance which is effective in shortening the coagulation time of the blood from the hemophiliac

SYMPTOMS The symptoms begin in infancy or childhood and are manifested by *habitual hemorrhage* which occurs spontaneously or from trauma There is a prolonged oozing of blood from cuts or wounds Hemorrhage from the lips, mouth, nose, gums, and tongue, or resulting from slight trauma or from the eruption and loss of teeth, takes place. Hemorrhage into the brain or spinal cord may result in transient or permanent paralysis and sensory disturbances. Hematuria from bleeding in the bladder or the kidneys may give rise to ureteral clots which produce severe colic

Hemorrhage into the joints as the result of the hemophilic process produces the hemarthrosis characteristic of the disease. The onset of the joint hemorrhage is sudden The joint is flexed, swollen, warm and painful Discoloration of the skin occurs only about small joints. The process is chronic and its symptomatology resembles that of a chronic infectious process. The ankle is frequently the joint earliest

begin and remain as a purpuric spot without swelling, but more often the lesions are multiple and accompanied by swelling Blebs may form which have the appearance of herpes with a hyperemic base or there may be bullae or even pemphigoid lesions Interspersed between lesions or associated with the purpura may be a *diffuse erythema*, with or without swelling.

The diagnostic features are the same as those for a nonthrombocytopenic purpura. There often is a leukocytosis with an eosinophilia. Identification of an allergin assures the correctness of the diagnosis.

Schönlein-Henoch Disease (*Nonthrombopenic Purpura*). Allergic purpura associated with gastrointestinal symptoms in children and adolescents is *Henoch's* purpura. *Schönlein's* purpura affects the periarticular structures of the joints of young adults.

In Henoch's purpura there is urticarial serohemorrhagic effusion into the intestinal wall In Schonlein's purpura there is a periarticular effusion into the joint which is not hemorrhagic

In Schonlein's disease the joints, often the knees, form periarticular effusions and there are pains in the limbs. There are purpuric spots over the legs. The joint manifestations and the hemorrhagic manifestations are commoner in the lower extremities than in the upper extremities.

SYMPTOMS The abdominal symptoms of Henoch's purpura may develop before any purpuric eruptions appear. Usually there is colic which varies from mild and transient to severe The pain is not localized, and occurs in all parts of the abdomen Vomiting, diarrhea or constipation, and tenesmus may occur. In some patients constipation may be so stubborn as to suggest intestinal obstruction In rare instances the purpuric gut may form intussusception Rheumatoid pains and fever may precede the attacks of abdominal pain and purpura.

In either or both of these purpuras involvement of the *nervous system* and *organs of special sense* may be revealed by the development of transient paresis and epileptiform convulsions The eyes may be affected by hemorrhages into the eyelids, conjunctivae or retinas Optic atrophy, iritis and ophthalmitis are the usual ocular involvements

Hematuria from renal involvement is rare.

EXAMINATION. General abdominal tenderness without rebound is present. The purpura may or may not be present on the first examination When it does occur, it is commoner over the lower extremities

The joints, particularly a knee, may be swollen, and purpuric spots may be present over the legs

Hemorrhage is rarely sufficiently marked to produce anemia. There may be neutrophilic leukocytosis, sometimes eosinophilia The blood platelets are not significantly affected, and bleeding time, coagulation time, and clot retraction are normal Results of the tourniquet test and the snake venom test may be positive or negative

The *urine* may be normal, or blood or albumin may be found. Examination of the stools may reveal blood

DIAGNOSIS Henoch's purpura is diagnosed when there are visceral manifestations; Schonlein's purpura, when there are joint manifestations. Before purpura or other skin manifestations have appeared, a diagnosis of either disease cannot be made. If purpura is present, the normal blood findings exclude thrombopenic purpura. The platelets are not reduced. Coagulation time and bleeding time and clot retraction are normal. The tourniquet reaction may or may not be positive

Purpura Simplex. Purpura simplex may be a hereditary disease or it may be acquired It is purpura without hematologic changes

Hereditary familial purpura simplex, as described by Davis in 27 families in

which there were spontaneous ecchymoses in 88 members, is similar to the form described by Giffen.

The diagnostic criteria for purpura simplex are the presence of mild purpuric skin manifestations unassociated with definite abnormalities in the blood. The tourniquet test is positive. Rheumatoid arthritis and rheumatic fever are frequently associated

Pseudohemophilia (Hereditary Hemorrhagic Thrombasthenia, Thrombasthenia Purpura). Pseudohemophilia belongs to the group of hereditary hemorrhagic diatheses. It is a hereditary disease with no predilection for sex. The disease has been considered to be due to a *congenital capillary dysplasia.* Others have considered the condition to be due to thrombasthenia, the platelets, however, are normal The disease may begin in infancy or at any time thereafter.

The clinical symptoms are similar to those of hemophilia There are recurrent nosebleed, hemoptysis, hematemesis, vaginal bleeding, hematuria and hemarthrosis The bleeding may follow slight trauma and may be mild or severe and in some instances fatal

On examination there often is neither anemia nor splenomegaly The blood cells and platelets are normal. The bleeding time is prolonged but the coagulation time is normal Thus the changes in the bleeding and coagulation time are the opposite from those present in hemophilia. The tourniquet test is positive

In diagnosis, the genealogic history signifies that the bleeding tendency is transmitted by both sexes The bleeding time is prolonged, but there are normal numbers of platelets and coagulation time is normal A family history of epistaxis may be accepted as evidence of the hereditary nature of the disorder.

Hemophilia. In hemophilia there is a permanent inborn defect which inhibits blood coagulation This defect is hereditary in origin and is sex-linked It is a recessive mendelian trait.

The disease is limited to the male but is transmitted from the male through an unaffected daughter to her son. The sons of an affected man cannot transmit the defect to any of their descendants. Only the daughters are capable of transmitting the trait Females never manifest the disease.

Long inheritance through females, with the males being insufficiently affected to manifest the disease, is an acceptable explanation of the occurrence of *sporadic cases* of hemophilia.

It has been well demonstrated that there is no lack of fibrinogen, no calcium deficiency, no reduction in number of platelets. The defect seems to be present in [illegible]

of the blood from the hemophiliac.

Symptoms The symptoms begin in infancy or childhood and are manifested by *habitual hemorrhage* which occurs spontaneously or from trauma There is a prolonged oozing of blood from cuts or wounds Hemorrhage from the lips, mouth, nose, gums, and tongue, or resulting from slight trauma or from the eruption and loss of teeth, takes place Hemorrhage into the brain or spinal cord may result in transient or permanent paralysis and sensory disturbances. Hematuria from bleeding in the bladder or the kidneys may give rise to ureteral clots which produce severe colic

Hemorrhage into the joints as the result of the hemophilic process produces the hemarthrosis characteristic of the disease The onset of the joint hemorrhage is sudden. The joint is flexed, swollen, warm and painful. Discoloration of the skin occurs only about small joints The process is chronic and its symptomatology resembles that of a chronic infectious process The ankle is frequently the joint earliest

involved. The knee is often permanently crippled. No joint can be said to be exempt from involvement by hemophilia

EXAMINATION. Mentally these patients are normal, often precocious. There is no enlargement of lymph nodes and the spleen is not palpable.

On examination of the site of the origin of hemorrhage the tissue is hard, indurated, raised and purplish black The hemorrhage at the site of origin may be entirely absorbed while the margin is still progressing to involve large areas of the body

Hematomas may involve areas in which the pressure may lead to gangrene. If sufficient pressure is exerted on a nerve, contracture may result (Volkmann's contracture)

Examination of the joints during the acute attacks reveals that the joints are swollen, tender and painful on active or passive motion. If the disease in a joint has been present for a few weeks and the swelling and tenderness are still present, the condition is beginning to be chronic. If acute attacks of hemarthroses are repeated from time to time, there is a permanently swollen joint with local deformity, contractures and muscular atrophy. Repeated hemorrhages in a large joint in time tend to cause less immediate increase in the size of the joint as the articular capsule becomes thickened and restricts swelling As chronicity progresses, the larger joints contain fibrous contractures and bony ankylosis. In the smaller articulations complete destruction of the joints takes place Atrophy and proliferation of bone and roughening of the articular surfaces with lipping and formation of osteophytes and cysts retard or stop growth

Other than the prolonged coagulation time, there is nothing characteristic in the blood

DIAGNOSIS. The task of making the diagnosis begins with the finding of a prolonged coagulation time if there is no history of repeated bleeding and familial occurrence A deep hematoma may resemble, on examination, a suppurative condition, a sarcoma, tuberculosis, arthritis deformans, Perthes' disease, or a syphilitic affection of the bone or joint Bleeding from the alimentary tract, despite the fact that the coagulation time of the blood is known, requires a differentiation from all those conditions known to produce such hemorrhages.

In the hereditary hemorrhagic diathesis, the bleeding time is prolonged Those who have familial epistaxis (pseudohemophilia) possess normal bleeding and coagulation times.

The diagnosis of hemophilia is based on the following findings present in a male. (1) prolonged coagulation time of the blood and of recalcified oxalated plasma, (2) normal clot retraction time after the clot has once formed, (3) normal bleeding time except at times of active hemorrhage when it is prolonged and (4) normal numbers of platelets, normal prothrombin time and variable degrees of anemia The tourniquet reaction is negative

In hemophilia death in time inevitably ensues from exsanguination However, some of these patients may live for years.

Anticoagulants as a Cause of Hemorrhage. Hemorrhage from anticoagulant therapy usually ensues (1) in persons taking dicumarol without medical supervision (or it may occur in patients receiving heparin therapy), (2) from poor laboratory control, (3) from overdosage by the physician, (4) from ill-advised surgical procedures and (5) from diagnostic errors, which account for the anticoagulant-induced hemorrhages and fatalities Ill-advised surgical procedures and diagnostic errors are not considered here.

The incidence of hemorrhage following the use of anticoagulants is increased if the dosage is pushed to the limit in the belief that it is more desirable to assure patients full protection against thrombo-embolic complications and thus run some

risk of hemorrhage, than to use a dose carrying with it so little chance of hemorrhage that it might fail to inhibit intravascular clotting.

An editorial in the Journal of the American Medical Association in 1950 revealed that data obtained from a questionnaire answered by 136 physicians experienced in the use of dicumarol and heparin indicate that major hemorrhage occurred in 2 per cent of about 15,500 patients treated The chief site of major hemorrhage was the urinary tract Gross hematuria occurred in 93 cases recorded in the questionnaire, but in no instance was it the cause of death although hematuria was associated with fatal bleeding in other sites in 3 cases Hematuria was not followed by residual renal impairment Most other instances of major bleeding were associated with pathologic lesions in the gastrointestinal tract or lungs or were in postoperative sites

In the "Report of the Committee for the Evaluation of Anticoagulants in the Treatment of Coronary Thrombosis With Myocardial Infarction" hemorrhagic complications occurred in 54 patients, or 9 per cent of the treated group; in half of them the condition was mildly severe An additional 6 per cent of the treated group had hemorrhage not due to anticoagulants, while in the control untreated group hemorrhage occurred in 6 per cent Hemopericardium was found in 11 of the treated and only 4 of the control group.

Bleeding induced by dicumarol is usually controlled by adequate amounts of water-soluble vitamin K or menadione bisulfite Transfusions of blood and plasma are of value after hemorrhage due to either heparin or dicumarol

Clinicians experienced in the use of anticoagulants agree there is less risk of hemorrhage with heparin than with dicumarol The Lee-White test of clotting time to control heparin therapy can be done by the average technician. Protamine sulfate, given intravenously, helps to correct the coagulation defect following heparinization Unless the available laboratory is well versed in the pitfalls of the prothrombin determination, dicumarol should not be used

The vagaries of the Quick test of prothrombin time necessitate special knowledge of the technic. False confidence may be inspired if the laboratory records the prothrombin time in percentage of normal To follow adequately the prothrombin response the normal range of the test as done by the available laboratory should be known and the dicumarol dosage should be adjusted in an attempt to maintain the prothrombin time between two and two-and-a-half times the average normal, expressed in seconds, obtained by identical technic with the same thromboplastin, in which event the percentage of prothrombin activity will fall between 10 and 30 per cent, a safe yet effective bracket Hemorrhage rarely occurs until the prothrombin activity is depressed to 5 per cent unless some pathologic lesion is present in the kidneys, gastrointestinal tract, lungs or brain

THE LYMPH NODES AND THE SPLEEN

In association with the regional diseases of the neck the usual causes for enlargement and disease of the lymph nodes were considered In that discussion it was mentioned that enlargement of the lymph nodes is commonly caused by infections opportunely situated Enlargement of spleen, lymph nodes, and occasionally the liver may result from infections which are blood borne but more commonly is due to causes other than infection

In the present discussion interest is in enlargement of the lymph nodes, the spleen and occasionally the liver in association with or as a manifestation of blood dyscrasias or primary disease of the lymphatic tissues

Malignant Lymphoma. Many generic terms are used to designate diseases of the lymphatic system characterized by progressive tumor-like enlargement of lymphoid tissue with eventual fatality, and histologically by multiplication of one or more of the elements normally present in lymph nodes to the point of destruction of the nodal architecture. The term malignant lymphoma is in general use and has the advantage of being noncommittal in regard to the cause for the enlargement.

In recognition of the complexity of the problem of nomenclature of malignant lymphomas the American Association of Pathologists and Bacteriologists established the "Registry of Lymphatic Tumors" and in 1934 set the seal of the registry's

approval on the schematization and terminology employed. The arrangement of data represented an attempted fusion of three classifications: (1) cytologic, based on morphologic recognition of component proliferating cells, (2) gross anatomic, depending on the distribution of the process throughout the organs of the body and (3) clinical, contingent on physical signs and hematologic manifestations

Hardly was the printer's ink dry on this classification before Gall and Mallory offered a somewhat different classification, because attempts to apply the registry's terminology convinced them that it is not practical for routine use. They presented a cytologic classification of malignant lymphomas and showed its advantages in a clinicopathologic survey They demonstrated by multiple examinations at significant time intervals that the cytologic type is remarkably constant, although a few cases show *a progressive failure of differentiation as the disease progresses. In* contrast, in a classification based largely on distribution, such features as the presence or absence of leukemia, generalization versus localization, and "sarcomatous" growth were considered important These have been shown to be inconstant and changeable, thereby requiring variation in classification from time to time in order to fit the stage of the disease The vast majority of Gall and Mallory's 618 cases from which histologic material was available could be readily divided into seven categories: (1) stem cell lymphoma, (2) clasmatocytic lymphoma, (3) lymphoblastic lymphoma, (4) lymphocytic lymphoma, (5) Hodgkin's lymphoma, (6) Hodgkin's sarcoma and (7) follicular lymphoma.

This classification differs from accepted classifications primarily in the subdivision into two types of what has generally been grouped under the heading reticulum cell sarcoma, one type in which the cells are highly undifferentiated and resemble lymphoid stem cells, for which the authors have proposed the name stem cell lymphoma, and a *second type in which the cells show recognizable features of differentiation in the direc*tion of tissue phagocytes, which they have termed clasmatocytic lymphoma It has also proved useful to divide the tumors showing clear evidence of belonging to the lymphocyte series of cells into lymphoblastic and lymphocytic types depending on whether the immature or the mature cells predominate. Hodgkin's disease too has appeared divisible into lymphomatous and sarcomatous types. Follicular lymphoma has been shown to be a form of malignant lymphoma and not, as has been claimed, merely an inflammatory process

The etiology of none of the malignant lymphomas is known, but the majority must now be regarded as neoplasms. Some investigators have considered Hodgkin's disease to be of an infectious origin; thus the terms lymphogranuloma, lymphogranulomatosis, lymphomatosis granulomatosa The malignant nature of Hodgkin's disease is indicated by the terms lymphosarcoma, reticulum cell sarcoma, giant follicular hyperplasia, round cell sarcoma, leukosarcoma, lymphadenosarcoma, lymphocytoma, monocytoma and pseudoleukemia

Often all of these diseases will be, as is done here, included under one heading The three general all-inclusive headings which may be employed are (1) malignant lymphoma, (2) lymphoblastoma and (3) lymphomatoid diseases

The clinical manifestations of these conditions are so nearly identical in some and so varied in others as to make differentiation on clinical findings impossible Differentiation can be made, but not always agreed on, by pathologists by histologic study Two general groups can be distinguished, namely, the reticulum cell sarcoma or the lymphosarcoma, and Hodgkin's sarcoma. These are histologic diagnoses; the use of terms designating cytologic diagnoses is avoided until biopsy has been made and the results have been recorded.

Lymphosarcoma and Hodgkin's Disease. By some observers Hodgkin's disease is divided into three types: (1) *Hodgkin's granuloma* is the common type of the disease The manifestations of the granuloma are protean and the condition is usually fatal within a few years (2) *Hodgkin's paragranuloma* is a comparatively benign condition beginning in almost all instances in the lymph nodes of the neck [illegible] nodes (see [illegible] as a (3)

comparatively localized tumor, develops rapidly, and results in death. These three types of Hodgkin's disease have in common the presence of Sternberg-Reed cells, and any one type of the disease may be transformed into another type.

From the standpoint of morphologic change in lymph nodes, there is no sharp distinction between leukemia and the forms of Hodgkin's disease

Hodgkin's disease has been regarded as a type of malignant disease different from most of the other cancerous processes Many of its characteristics suggest an inflammatory origin. The possible infectious characteristics of Hodgkin's disease have been reexamined by the previously unused technic of serial passage of the Hodgkin's disease lymph-node extracts in embryonated chicken eggs A slight lethal effect in the embryos ensues The amniotic fluid collected after numerous serial passages from Hodgkin's disease-inoculated embryos has certain filtrable, transferable, and virus-like properties.

Hodgkin's disease affects a younger age group than do the other lymph-node disorders The average ages vary from 36 to 50 years In all forms of the disease men are more frequently affected than women.

SYMPTOMS The various diseases chiefly affecting lymph nodes produce similar symptoms A lymph-node enlargement is the usual complaint

The general symptoms of Hodgkin's disease are widely varied and, for instance, may resemble those of tuberculosis or undulant fever. Tachycardia may be observed which is out of proportion to the degree of fever and thus may be remindful of thyrotoxicosis

The absence of general symptoms early in the course of lymphosarcoma is in contrast to Hodgkin's disease in which, in the common granulomatous type, constitutional symptoms appear early. In children Hodgkin's disease is prone to be characterized by a prolonged period of fever. The fever may be moderate, irregular and continuous In adults too a fever may last weeks or months with afebrile periods of variable duration In a few patients the temperature ranges to 104 F (40 C) or higher In about 1 of every 16 there is irregular, remittent, or continuous pyrexia of several days' to several weeks' duration interrupted by periods of remission. This pyrexia is termed Pel-Ebstein fever or alternating pyrexia

The intensity of the pruritus, often with little or no objective cutaneous manifestations, is maddening, and the suffering from this symptom may be indescribable.

Bone symptoms and anemia are varied and consist of pain and weakness.

Urogenital symptoms are present in about one third of cases. These symptoms result from invasion or from pressure The urinary symptoms are hematuria, pyuria, retention of urine, pain in the back, a mass in the flank, or symptoms indicative of disease of the prostate gland or of the testicles

Paresthesias and pain are common complaints which have a neurologic origin

EXAMINATION The intensity of the pruritus in an occasional case of Hodgkin's disease is evidenced by scratch marks and obvious irritation of the skin A brownish, localized or generalized pigmentation of the skin may accompany pruritus or appear independently of it In Hodgkin's disease, erythema, a macular morbilliform eruption, herpes zoster, eczema, papules, wheals, vesicles, bullae, furuncles, and lichenification occur Ulceration may follow necrosis of lymph nodes or cutaneous tumors

Firm intracutaneous nodules, colorless or shiny bluish red, are the commonest specific lesions in lymphosarcoma However, similar lesions may be present in Hodgkin's disease.

Involvement of superficial nodes is present in almost all those who have one of these lymph-node disorders In rare instances of Hodgkin's disease, however, no involvement of lymph nodes has been found at necropsy.

The nodes of the neck are usually the first affected in Hodgkin's disease and in the "sarcoma" group. In Hodgkin's disease primary mediastinal and abdominal adenopathy may be found. The lymph-node enlargement is along the sternocleidomastoid muscles and in the supraclavicular spaces, often forming a large, irregular, nodular, collar-shaped tumor over the anterior lower portion of the neck

The common lymph-node involvement of the neck, nasopharynx and tonsils was discussed in Chapters 4 and 5. Hodgkin's disease and other lymph-node tumors which invade the mediastinum and lungs were described in Chapter 9. May it be repeated here that chylous effusion is much commoner in the diseases chiefly affecting lymph nodes than as the result of any other cause, and of these it is most frequent in follicular lymphoma.

In follicular lymphoma (Mallory) gastrointestinal involvement is rare but may occur. Ascites is frequent and is often chylous in this disease In Hodgkin's disease the gastrointestinal tract is rarely affected, but it may be exclusively involved The digestive symptoms may be due to enlargement of lymph nodes or may arise from the systemic febrile effects of the disease (Pel-Ebstein).

Digestive symptoms are due to the presence of enlarged lymph nodes or are the result of systemic effects in the late stages of these lymph-node diseases. Gastric lymphosarcoma occurs and is a rare malignant gastric tumor. The average age incidence of gastric sarcoma of the Hodgkin type is lower than that of gastric carcinoma The symptoms are similar to those of carcinoma or peptic ulcer.

The liver and spleen may not be enlarged Those seriously ill of the disease, however, often have splenic enlargement

In the intestines the frequency of occurrence decreases distally, except that the rectum is involved more often than the colon The lesions may be polypoid, protruding into the lumen of the intestine, annular, or diffuse, and infiltrating the wall of the bowel

Bone lesions are often demonstrated by roentgenograms in Hodgkin's disease, lymphosarcoma, and rarely in monocytoma The lesions are found most frequently in the pelvis, vertebrae, ribs and femora, but other bones may be involved In most cases more than one bone is affected

Paresthesias and pain are the commonest neurologic findings Herpes zoster is often the cause of the pain Diplegia as the result of circulatory disturbances of the spinal cord, or due to collapse of involved vertebrae producing angulation and compression of the cord, is unusual Pathologic fractures rarely occur

There are no *blood changes* in these disorders which can be considered as diagnostic of Hodgkin's disease

The value of bone marrow study in the diseases which chiefly affect lymph nodes is to exclude leukemia (the aleukemic form)

The basal metabolic rate is frequently increased. The uric acid content of the blood may be considerably increased The alkaline serum phosphatase, if persistently elevated, may indicate bone invasion

In Hodgkin's disease the erythrocyte sedimentation rate may be accelerated or may be normal

Diagnosis The diagnosis of all of the diseases affecting the lymph nodes is established by biopsy of an enlarged node

The problem of diagnosis is much more difficult when the primary lesion does not affect one of the superficial groups of lymph nodes, for then the symptoms may attract attention to any of the systems of the body and may mimic any one of a great many diseases Thus there may be chronic dermatitis The cutaneous manifestations may be accounted for only on histologic study of the skin There may be a tumor of the bowel; the onset may be characterized by *melena or hematemesis* or ascites The symptoms may suggest pulmonary tuberculosis, bronchogenic carcinoma, septicemia, endocarditis, typhoid fever, rheumatic fever, pyelitis, prostatic disease or some neurologic disorder

The factors which determine the course of the illness in individual cases are

amination of the blood. This condition is often termed pseudoleukemia, aleukemic leukemia or small cell lymphosarcoma Clinically the manifestations are the same as those of Hodgkin's disease Histologic study is required for diagnosis.

Reticuloendothelial Granulomatosis. The reticuloendothelial system contains cells with endothelial and reticular attributes and showing a common phagocytic behavior. These cells are distributed in the spleen, lymph nodes, liver (Kupffer's cells), bone marrow and the clasmatocytes. Reticuloendothelial cells are concerned with blood cell formation, the storage of fatty materials, phagocytic destruction of blood cells and the metabolism of iron and pigment

Well informed pathologists and clinicians may regard what may seem to be, from the standpoint of the clinician, a form of lymphosarcoma or a Hodgkin's disease as reticuloendothelial granulomatosis Two diseases named after men who first described them may be given as examples. Hand-Schüller-Christian disease and Letterer-Siwe disease

Hand-Schüller-Christian disease is a systemic reticuloendothelial granuloma of unknown origin The disease may exist in a widely disseminated form characterized by reticuloendothelial granulomas in many parts of the body, or it may be a more limited granulomatosis occurring, for instance, in the ribs, skull or other bones and the lungs. The individual granulomas present may fail to exhibit the characteristics of foam cells and cholesterol crystals Usually, however, there are large foam cells present. The nonlipid granulomas usually involve the bone marrow, lymph nodes and spleen The replacement of the blood-forming marrow tissue with the granulomas is responsible for the anemia (see Myelophthisic Anemia, page 843) which is often the most conspicuous manifestation In some instances of so-called Letterer-Siwe disease the spleen, the lymph nodes and the vertebral marrow are entirely free of granulomas

The phagocytic properties possessed by the reticuloendothelial cells are manifested by the tendency to contain quantities of hemosiderin pigment obtained from nearby hemorrhages present in the lymph nodes, bone marrow or spleen

There is a progressive enlargement of the granulomas, lymph nodes and often the spleen With the onset of necrosis in the lesion the cholesterol is liberated from the cells and it may be absorbed into the blood stream and give rise to transient hypercholesteremia However, the value for serum cholesterol is usually normal

Letterer-Siwe disease is a form of xanthomatosis characterized by great hypertrophy of the macrophages in the spleen, bones and lymph nodes These cells are devoid of lipoid substances.

THE SPLEEN

On examination of the abdomen the spleen may be found to be enlarged without any recognizable accompanying symptoms At this point it is well to enumerate at least some of the causes for splenic enlargement Some are common causes and others are uncommon, and probably this listing is not complete

CAUSES OF SPLENOMEGALY

1. Infectious·
   a Acute fever, septicemias, pyemias, formation of abscess with splenic abscess, bacterial endocarditis and disseminated lupus erythematosus
   b Chronic syphilis and tuberculosis
   c Parasitic infections malaria, leishmaniasis, trypanosomiasis, schistosomiasis and echinococciasis
   d Infectious mononucleosis
2 Circulatory (often mechanical)·
   a. Cirrhosis of liver, Banti's disease, thrombosis of either the portal or splenic veins as a complication of cirrhosis or any other circulatory cause of thrombosis
   b. Congestive splenomegaly—heart failure

3. Hemic and lymphatic.
   a Chronic hemolytic anemias.
   b Chronic anemia with or without blood destruction.
   c Purpura haemorrhagica.
   d. Benign lymphatic hyperplasia.
   e. Malignant hyperplasia. leukemias.
   f. Polycythemia vera

4. Metabolic
   a Gaucher's disease
   b. Niemann-Pick disease
   c Schuller-Christian disease.
   d. Amyloidosis.
   e Diabetic lipemia, hyperthyroidism

5. Tumors
   a Cysts dermoid and pseudocysts.
   b Benign tumors: hemangioma, lymphangioma, fibroma.
   c. Follicular lymphoma, monocytoma, reticulum cell sarcoma, Hodgkin's lymphoblastic and lymphocytic lymphoma
   d Primary and metastatic malignant lesions.
   e Boeck's sarcoid

Banti's Disease (Congestive Splenomegaly) At this place it is wel sider the disease variously known as *Banti's disease, splenic anemia, an* congestive splenomegaly

The disease may come on in childhood Females were twice as num males in Banti's series and this was true of Giffin's series but has not been in all reports. A familial incidence is rare but is not unknown

Congestive splenomegaly and the accompanying changes of Banti's synd now considered to develop as a result of any pathologic process. congenital matory, neoplastic, parasitic or fibrotic, which interferes with the flow of por through the liver or at any point in the splenic or portal vein In the majority the obstruction is only partial and has developed gradually Thrombophlebi *splenic or portal veins, portal cirrhosis, and cirrhosis due to schistosomiasis are* monest causes of obstruction Obstruction in the mesenteric veins leads to f of varicosities and to intestinal bleeding, but unless the portal or splenic veins involved by extension, the obstruction will not produce congestive splenomega

The spleen is enlarged The capsule is thickened, and adhesions between th and the stomach or diaphragm may be present On section the spleen is gra and firm The trabeculae are prominent and malpighian bodies are inconspicu

The hemorrhagic tendency is due both to local and to systemic causes affec portal system. The walls of the veins of the portal system are stretched and particularly those of the distal portion of the esophagus and sometimes thos rectum The mucosa overlying the distended veins is thinned and eventually a process which contributes to the erosion of the wall of the underlying vein

The thrombopenia and hypoprothrombinemia present in this syndrome de *prompt formation of effective blood clots at points where small ruptures of t* have occurred

SYMPTOMS. The onset is usually insidious and there may be only a s heaviness or fullness in the upper part of the abdomen In some instances th may come with suddenness, when vomiting of blood or the passage of larg stools takes place *in a patient who is otherwise in good health* In other in abdominal pain or discomfort, or symptoms of weakness and a general la referable to anemia bring the patient to the physician Flatulence, diarrhea, indigestion, or even mild jaundice in association with abdominal pain and may appear. Epistaxis occurs in about a third of the cases, but other hemo ... such as purpura are *unusual*.

EXAMINATION. A brown pigmentation of the skin may be present. The spleen is large and may extend to the pelvis Moderate hepatic enlargement has been observed at an early stage in perhaps a third of the cases. Lymphadenopathy is absent.

Endoscopic examination is attended with small risk in the experienced hands. This examination helps to identify the varicosities and to determine their approximate size when they are situated in either the esophagus or rectum.

Roentgenographic study of the esophagus when filled with barium may reveal varices in that situation

Splenomegaly may precede anemia which, unless hemorrhages have occurred, is moderate and, as a rule, normocytic. Repeated hemorrhages result in hypochromic microcytic anemia. Subsequent to a hemorrhage the reticulocytes may be slightly or moderately increased in number, and occasional normoblasts may be observed A macrocytic anemia may appear temporarily following an acute hemorrhage

Leukopenia is constant except after hemorrhages. Leukocyte counts less than 5,000 per cubic millimeter have been observed in about two thirds of the cases The diminution of the leukocytes often affects all the types of cells, the ratio of the polymorphonuclear leukocytes to the lymphocytes and monocytes remaining normal.

The platelet count is often somewhat reduced, and sometimes it is well below 100,000 per cubic millimeter

Sternal puncture reveals varied conditions in the bone marrow In the earliest stages of the syndrome, the bone marrow is hyperplastic, especially the erythropoietic series If there is thrombopenia, it may be difficult to differentiate the syndrome from idiopathic thrombopenic purpura In the later stages, when there are ascites and severe impairment of hepatic function, the bone marrow may be hypoplastic.

DIAGNOSIS A diagnosis of Banti's disease depends on elimination of hemolytic jaundice, aleukemic leukemia, and bleeding from peptic ulcer The presence of lymphadenopathy or of immature leukocytes in the blood smear favors conditions other than Banti's disease. The presence of decreased hepatic functional activity favors Banti's disease The diagnosis of the disease is made more nearly certain by the presence of esophageal varices. Persistent leukopenia and thrombopenia, with little or no alteration after hemorrhage are characteristic manifestations of Banti's syndrome

The disease may run a prolonged and often benign course and may appear to be spontaneously arrested, the patient living for a number of years without disability. At any time, however, the uneventful course may be interrupted by one or more episodes of gastrointestinal hemorrhage, portomesenteric venous thrombosis or hepatitis In other instances there is steady progression with the development of symptoms of hepatic insufficiency and the signs of portal venous obstruction and death. In some instances death follows a hemorrhage or some other complication

Rupture of the Spleen. Rupture of the spleen may occur from nonpenetrating trauma Such a rupture may cause primary or delayed hemorrhage It is suggested that changes in the hematoma, whether subcapsular or perisplenic, may be a factor in delayed hemorrhage and may account for the majority of ruptures occurring on the sixth or seventh day after trauma

It is important to attempt to obtain a history of trauma in every case of sudden pain in the upper left quadrant of the abdomen running occasionally to the left shoulder. The injury may have been slight or have occurred a week or more previously and to the patient it may seem too insignificant to be mentioned

The difficulty in making an early diagnosis is one of the most important causes of the high mortality rate from rupture of the spleen The syndrome of delayed hemorrhage is most difficult to detect The hemorrhage is delayed in about 20 per cent of the cases, with a latent period on the average of about 6 days from the time of injury to the onset of a massive hemorrhage. Cases with latent periods as long as

6 months have been reported. Roentgenologic diagnostic signs and abdominal paracentesis may aid in establishing the diagnosis of injury of the spleen in cases of delayed hemorrhage.

LEUKOCYTES

In the blood there are: (1) mature neutrophilic leukocytes, which have segmented or filamented structures, (2) immature neutrophilic leukocytes without filamented or segmented structures, (3) eosinophils, (4) basophils, (5) lymphocytes and (6) monocytes

In normal blood the *total leukocyte count* ranges from 5,000 to 10,000 per cubic millimeter Variations in number as great as this may be observed in the blood of the same normal individual from day to day, and wide daily variations may occur.

The leukocytes are made up of three distinct groups of cells which differ from one another fundamentally in origin, in structure, and in function: the granular (myeloid) leukocytes or granulocytes, the lymphocytes, and the monocytes

The *granulocytes or myeloid* cells contain definite granules which are visible in fresh as well as in stained preparations. In normal blood there are three varieties, distinguished by the staining reaction of the granules: neutrophils, eosinophils (acidophils), and basophils

Immature granulocytes, the ancestors of the aforesaid types of cells, may appear in the blood in certain pathologic conditions. Normally some mechanism prevents the passage of cells into the blood before they are mature It is the phenomenon of their entrance into the blood stream, and not the character of the cells themselves, which is pathologic The presence of the pathologic process, however, is manifested by the presence of these immature cells in the blood stream In general, the more numerous and *the less mature these cells are, the more serious is the disturbance of the hematopoietic tissue*

Lymphocytes or *lymphoid cells* arise from the fixed lymphatic tissues In the normal circulating blood two types of lymphocytes are differentiated, namely, large and small lymphocytes The small lymphocytes comprise 20 to 30 per cent of the leukocytes in the peripheral circulation

Immature lymphocytes, like the immature granulocytes, in the presence of certain diseases may pass into the circulating blood The more immature *the lymphoid cell is,* the more serious is the disease causing the immature cells to appear in the circulating blood

Plasma cells are present in small numbers in the bone marrow but rarely are they observed in the peripheral circulation The exact origin of these cells is unknown

Turk's irritation leukocytes may be observed in the circulating blood if there be an irritating lesion of the bone marrow or a disease of the lymphoid tissues.

The consensus is that *monocytes* are a separate series of cells They arise *from reticular* cells of the reticuloendothelial tissues In a mature form they comprise 4 to 5 per cent of the cells of the circulating blood.

Leukocytosis. The term leukocytosis signifies an increase in the total leukocyte count (more than 10,000 per cubic millimeter of blood) In most instances leukocytosis is due to an increase in the neutrophils, and thus the term neutrophilic leukocytosis may be employed if the neutrophils predominate. A leukocytosis is called relative if the total leukocyte count is within normal limits, but the percentage of neutrophils is increased to more than 70 per cent of the total count. The term absolute leukocytosis is employed if the total number, as well as the relative number, is increased The terms relative leukocytosis and absolute leukocytosis are of little value in diagnosis except when there is an absolute leukocytosis

OCCURRENCE. Normal persons may show a neutrophilic leukocytosis (1) after muscular activity (sometimes marked) and convulsions and (2) after *cold baths* or exposure to cold. There may be (3) leukocytosis in infants during the first few

days and (4) slight leukocytosis in pregnancy during the last few weeks and in the puerperium (sometimes marked, up to 20,000)

Neutrophilic leukocytosis occurs in most acute infections, particularly acute pyogenic infections The leukocyte count in acute pyogenic infection usually ranges around 15,000 per cubic millimeter; in lobar pneumonia it may reach 30,000 to 40,000

In many instances of acute poisoning, such as by heavy metals, and by drugs such as acetanilid and digitalis, the counts may reach 20,000 per cubic millimeter. In acute gout, in diabetic acidosis and in uremia leukocytosis may be present A leukocytosis follows acute hemorrhage and acute hemolysis of erythrocytes, surgical operations, coronary thrombosis, pulmonary infarction, and burns. The greatest increases in the leukocyte counts are observed in the leukemoid reactions and in the leukemias

SIGNIFICANCE Leukocytosis occurs when there is an increased demand for leukocytes The degree and type of response vary greatly and often unaccountably. In interpreting the leukocytic counts, changes in the differential count and qualitative alterations in the leukocytes are more significant than an increase in their total number Particularly, more reliable information is obtained by a study of the neutrophils from the standpoint of their maturity An increased demand is met by the production of new cells by the bone marrow When leukocytes are hastily liberated from the bone marrow many of the cells are carried into the circulation before development is completed

Arneth measured the phenomenon of immaturity of leukocytes by accepting the degree of segmentation of the nucleus as a criterion of maturity In making differential counts he divided the neutrophils into five groups The first group included all cells with unsegmented nuclei, and the second to the fifth groups (inclusive) comprised cells with nuclei composed of two to five lobes respectively. In instances of active infection the relative number of cells containing one or two nuclei was increased, and as these happened to be recorded on the left hand side of his tally sheets, this change was termed a *shift to the left* The term a shift to the left is frequently employed by hematologists to indicate an increase in the cells with unsegmented nuclei or a decrease in the number of cells with segmented nuclei Arneth regarded the shift to the left as far more significant than a rise in the total leukocyte count Arneth's method of counting is no longer employed in the laboratory The method now used varies with the individual hematologist, but often it is some modification of the method of Schilling

In general, in a severe infection there is an increased total leukocyte count with a high percentage of neutrophils, or there may be a complete failure to develop a leukocytosis, so that a leukopenia is present The immature cells outnumber the mature cells, eosinophils are absent, lymphocytes are reduced in number, and many cells show toxic-degenerative changes in the nucleus or cytoplasm The most valuable diagnostic and prognostic information is gained from repeated counts and studies of the cells to determine the directional trends in the forementioned changes in the leukocytes A single examination is often inconclusive and may be misleading.

Eosinophilia. The eosinophils normally comprise 2 to 4 per cent of the leukocytes They decrease in numbers during an acute infection but may return in increased numbers during the convalescence The term eosinophilia designates increases of more than 8 or 10 per cent Eosinophilia occurs chiefly (1) in *infection with animal parasites,* (2) in extensive *skin diseases* of any type; (3) in *allergic reactions,* (4) in chronic myelogenous leukemia and occasionally in Hodgkin's disease, (5) with certain tumors of the ovary, and in Cushing's syndrome, (6) in focal lesions of the bone marrow, and after splenectomy, (7) *in pernicious anemia* after liver therapy Irregular response of eosinophils occurs in adrenocortical insufficiency (see Addison's Disease, Chapter 14).

Eosinophilia in Tropical Disease. Lowe and his colleagues have expressed the belief that in malaria and in the helminth infections two different factors are con-

cerned with the production of eosinophilia: (1) a nonspecific factor similar to *that present in bacterial infections and* (2) *a specific factor* due to helminth infection.

Basophilia. The basophils normally comprise 0 5 to 1 per cent of the leukocytes. A basophilic leukocytosis occurs commonly in chronic myeloid leukemia. In other conditions it is infrequent and of no known diagnostic significance.

Lymphocytosis. The lymphocytes comprise 25 to 35 per cent of the total leukocyte count. *The majority of the lymphocytes in normal blood are the small variety.*

A *relative lymphocytosis* occurs in most of the conditions which show a leukopenia

An *absolute lymphocytosis* occurs in certain infections for instance, in whooping cough, and in tuberculosis of mild or moderately active degree running a favorable course. It *occurs less regularly in certain viral or viral-like infections such as* German measles, mumps, infectious mononucleosis and acute infectious lymphocytosis Lymphocytosis occurs during convalescence from any acute infection, after exposure to ultraviolet radiations, and in lymphatic leukemia. The regular occur*rence of lymphocytosis following acute infections may well be related to the devel*opment of immunity.

The lymphocytes, specifically, produce antibodies. By chemical fractionation of human plasma a large proportion of the antibodies is found to reside in the alpha, beta, and gamma globulins. The gamma globulin is present in the human lymphocyte.

Acute infectious lymphocytosis is a clinical entity characterized by a benign relative and absolute increase in the number of mature lymphocytes.

Smith has summarized the data for the establishment of acute lymphocytosis as a specific entity and differentiated it from infectious mononucleosis, acute lymphatic leukemia and miscellaneous infections associated with a lymphocytosis

In most of the reported instances of the disease the patients had been children, until Duncan reported 2 instances in which the patients were young adults

In most cases the disease is uncomplicated and has a uniformly favorable outcome The clinical manifestations are usually mild or absent. There is neither lymphadenopathy nor splenomegaly, and in all instances the heterophil antibody reaction is negative. The maximal leukocyte counts which have been observed range from 45,000 to 50,000 per cubic millimeter of blood with *85 to 90 per cent* lymphocytes. The lymphocytosis may persist for a period of approximately 3 to 5 weeks.

Monocytosis. Under normal conditions monocytes comprise from 5 to 10 per cent of the leukocytes

Monocytosis may occur in malaria and other [illegible] and is of less regular occurrence in certain viral and rickettsial [illegible] sis may be present in Hodgkin's disease, Banti's [illegible] thane, and monocytic leukemia

A slight increase in monocytes occurs frequently at the height of many acute infections.

Infectious Mononucleosis. This disease is known also as glandular fever, acute benign lymphoblastosis, acute lymphadenosis, monocytic angina and lymphocytic angina.

Infectious mononucleosis is an acute disease characterized by irregular fever, sore throat, often cervical lymphadenopathy, and enlargement of the spleen, and lymphocytosis with abnormal though mature lymphocytes The blood serum contains antibodies against sheep erythrocytes in high concentrations

The disease is cosmopolitan in distribution It appears sporadically and epidemically. The cause is unknown. It seems to be a specific infection. Those who have the disease are known to respond to other infections with the usual polymorphonuclear reaction Cocci, bacilli, viruses, spirochetes and protozoa all have been suspected as *etiologic*

agents but none has been proved. The disease has been thought to be a "lymphatic form" of influenza

The epidemic form occurs in the spring in children and young adults Boys and men are somewhat more susceptible than girls and women. It has been observed that epidemics of influenza in adults may be associated with outbreaks of infectious mononucleosis in children There is no seasonal incidence of sporadic cases. The contagiousness of the disease, if there be such, is low

The incubation period is uncertain, but the best evidence suggests that it is about 11 days

SYMPTOMS. The onset is characterized by fever and aching legs and back Anorexia is commonly present.

Sore throat if present may precede, accompany or follow the onset The throat may be diffusely reddened and a membrane may form Vincent's infection is a common complication. The gums often become tender, swollen and ulcerated and may bleed Epistaxis, hematuria, and rectal bleeding may occur

The temperature may reach 103 to 104 F (39 4 to 40 C), but often the fever is transient and slight A second rise of temperature may occur after an initial drop to normal. Synchronously with this second fever, lymph nodes in the neck are swollen and the throat is sore The fever may be intermittent. The pulse may be relatively slow A certain amount of toxemia is common In some cases the toxemia is severe and prostration supervenes Headache with the fever is often severe.

In some who have this disease there is a continuous feeling of fatigue associated with no abnormal physical findings

The course and duration of the disease are variable The irregular fever usually persists for 1 to 3 weeks, and symptoms disappear in 2 to 4 weeks but may continue longer. Recrudescences are common Adenopathy, splenomegaly and the characteristic blood findings may persist for months, even for years There is often a long period of slight but definite debility following an attack of infectious mononucleosis

Jaundice may develop in from 5 to 14 days after the onset of symptoms and may be the presenting symptom Hepatitis without jaundice occurs Nausea, vomiting, diarrhea and abdominal pain are fairly common symptoms, with or without jaundice. In children convulsions, stupor and coma may occur at the onset.

EXAMINATION Cutaneous eruptions may be present on the face, trunk and arms and may appear from the fourth to the tenth day in a few who have high fever with the disease The lesions are described as pink or pinkish brown, macular or maculopapular lesions 2 to 5 mm in diameter which may fade on pressure, as well as petechiae and hemorrhagic rashes Erythema nodosum and urticaria are described for this disease

An enlargement of the lymph nodes often develops rapidly Commonly the nodes posterior to the sternocleidomastoid muscles and epitrochlear nodes are affected The nodes are discrete, firm and elastic in consistency and are slightly tender They vary in size from ⅖ to 1⅗ inches (about 1 to 4 cm.) in diameter. Axillary and inguinal lymph nodes are usually not enlarged Thoracic or mediastinal lymph nodes may be found on roentgenologic examination to have increased in size, and pressure symptoms may be present

The spleen is palpable in more than one half of those who have the disease. The liver is less frequently palpable Petechial hemorrhages and purpura may be observed in the skin and mucous membranes.

From involvement of the central nervous system the heart rate may be slow, the neck stiff, and a positive Romberg sign and plantar extension may be present Examination sometimes reveals partial ocular motor paralysis, facial paralysis, cutaneous hyperesthesia and signs of diffuse involvement of the lower motor neurons

The characteristic finding in the blood is an increase in mononuclear cells consisting of small lymphocytes, monocytes and large mononuclear leukocytes which

are not normally observed in the blood The increase in numbers of these cells often occurs at the expense of the neutrophils.

The total leukocyte count is usually 10,000 to 15,000 per cubic millimeter but it may be normal or even lower than normal. In half of the cases there is leukopenia during the first week of the disease

The finding of anemia makes the diagnosis of infectious mononucleosis highly improbable. The platelet count is usually normal but thrombocytopenia has been observed. The bleeding time may be prolonged without relation to the platelet count.

When there is jaundice, the van den Bergh reaction is positive, delayed or direct biphasic and bilirubin is as high as 8 to 10 mg. per 100 ml.

Reaction to the serologic tests for syphilis may become transiently positive in a number of cases, and occasionally this may persist for several months. This effect is independent of the presence of sheep cell antibodies, for the positive reaction can be demonstrated in equally high titer even when the sheep cell antibodies have been absorbed out A falsely positive Widal reaction and significant increases of agglutinins for a variety of organisms have also been observed

Albumin and erythrocytes may be found in the urine A gross hematuria may be present Renal function is unimpaired.

The cerebrospinal fluid pressure may be moderately increased. Usually only a few or no cells are present in the fluid, but in a few instances pleocytosis has occurred, with as many as several hundred cells, mostly lymphocytes, present. The sugar content is normal, the protein may be increased and the reaction to the Pandy test may be strongly positive

The serum in those who have infectious mononucleosis contains agglutinins against sheep erythrocytes in high titer, a finding which has proved to be very useful in diagnosis (heterophil antibodies) The heterophil sheep cell agglutinin test often helps to confirm the diagnosis While sheep cell agglutinins are present in normal human serums, especially in patients undergoing serum therapy or suffering from serum sickness, when the antibody titer is higher than 1 64, it is said to be strong evidence of the presence of infectious mononucleosis Gardner and Paul in an analysis of the records of 86 cases studied in the New Haven Hospital found that reaction to this test had been positive in only 60 per cent of the cases, even at the height of the disease. The absence of the heterophil reaction, in some, may be explained by the fact that the sheep cell agglutinins reach a peak rapidly during the first week of the disease and may decrease just as rapidly in some instances

Sternal puncture is of value chiefly to reveal no findings characteristic of leukemia

Diagnosis. In all other blood disorders reaction to the heterophil antibody (Paul-Bunnell) test is negative In leukemia the titer of heterophil antibodies is particularly low The Paul-B[illegible]

The physical findings may [illegible]
be made in the absence of [illegible]
phenomena and immature leukocytes Moderate or severe anemia is almost always present when acute leukemia is first discovered

The greater age of the patients, the history of ingestion of drugs, and the absence of lymphadenopathy or splenomegaly are valuable differentiating features in agranulocytosis.

Infectious Mononucleosis and Benign Lymphocytic Meningitis. It seems that the clinical symptoms, course and prognosis of benign lymphocytic meningitis and of the neurologic manifestations of infectious mononucleosis are indistinguishable. The changes in the cerebrospinal fluid are identical in the two conditions In infectious mononucleosis with neurologic manifestations the enlargement of lymph nodes is usually slight This feature, together with mononucleosis and heterophil agglutinins, may develop only after the neurologic symptoms have subsided or may precede the nervous stage With the presence of such neurologic symptoms, infec-

tious mononucleosis can be excluded only by repeated attempts to demonstrate heterophil antibodies in the blood.

Infectious Mononucleosis and Polyneuritis (*Guillain-Barré Syndrome*). Polyneuritis of the Guillain-Barré type with facial diplegia, extensive peripheral neuropathy and albuminocytologic dissociation of the cerebrospinal fluid may be associated with infectious mononucleosis The neurologic manifestations are those of polyneuritis and the so-called Guillain-Barré syndrome, as evidenced by the multiple involvement of peripheral nerves and an ascending type of paralysis, with spinal fluid which contains a high protein content and no cells.

Leukemoid Reactions. The term leukemoid reaction is applied to a leukemia-like reaction of the leukocytes as a result of an infection or other stimulus. Such a reaction may be granulocytic, lymphocytic, or monocytic depending on the type of cell involved The reaction may be manifested by an exceptionally high total leukocyte count with the appearance of a few or many immature cells or by a great many immature cells without a great increase in the total leukocyte count A leukemoid reaction is commoner in children than in adults and is more frequently due to an infection than to other forms of marrow stimulation.

Leukopenia. A reduction in the leukocyte count to less than 5,000 per cubic millimeter of blood must be mainly at the expense of the neutrophils. It occurs regularly in typhoid fever, measles, influenza, dengue, kala-azar, malaria, the initial stages of smallpox, and extensive glandular tuberculosis It may occur in overwhelming infections, malignant neutropenia (agranulocytic angina), and in primary splenic neutropenia. Leukopenia occurs in acute or chronic poisoning from benzol, acetanilid, the sulfonamides, aminopyrine, lead, mercury, arsenic, thiouracil, dinitrophenol, and occasionally from barbiturates. It occurs after excessive radiation, in idiopathic aplastic anemia, leukemia, and in pernicious and myelophthisic anemias.

A leukopenia of 3,000 to 5,000 per cubic millimeter is commonly observed in apparently normal individuals The differential count may be normal, or there may be a slight relative lymphocytosis

Agranulocytosis. Agranulocytosis is known also as agranulocytic angina, granulocytopenia, granulopenia, agranulosis, agranulocythemia, hypogranulocytosis and idiopathic, malignant or pernicious leukopenia

In the infections known to be associated with leukopenia, granulocytopenia of the degree seen in agranulocytosis is rare The most important known cause is drugs.

The drugs which may produce granulocytopenia are benzene, organic arsenicals, gold salts and coal-tar products (see Diseases Due to Chemical Agents, Chapter 19) *The effect on the blood may be a selective one producing only granulocytopenia.* However, the granulocytopenia is often accompanied by a thrombocytopenia and an anemia These changes in the blood are not usually observed after one or two doses except in large doses of some of the organic chemicals The drugs usually have been administered over long periods of time before causing agranulocytosis

It is evident from daily observation that only a small proportion of persons consuming drugs suffer any ill effects

the blood generally appears only after a relatively large amount has been taken for a relatively long period Thus even after full dosage of one of the sulfonamide compounds, acute agranulocytosis has not developed before one week and usually not before two weeks of treatment Exceptions to this rule, in which leukopenia has developed within 24 hours after the ingestion of the usual therapeutic dose, are rare

Watkins encountered 17 cases in which a *barbiturate* (amytal, phenobarbital, luminal) appeared to be the cause of agranulocytosis

The use of *thiouracil* for the treatment of hyperthyroidism has added to the list of agents producing granulocytopenia.

The drugs which may produce agranulocytosis often cause other manifestations of idiosyncrasy, such as rash, urticaria, edema and asthma The fever, chills, headache and dizziness which have been noted in sensitive persons after administration of the drug suggest an allergic process

SYMPTOMS. The first symptoms are often malaise, fever and perhaps a chill Then follows a period of freedom from symptoms except for fatigue and prostration, and during this time the leukocyte count falls and the granulocytes disappear Several days or longer may pass after these premonitory symptoms and then there is a sudden severe chill and high fever with postrigor prostration.

In those who have a milder degree of the affection, the disease is a less fulminating one When the disease is chronic and recurrent, there may be vague symptoms such as headache, malaise, dizziness and exhaustion, and in some an actual prostration. There may be painful deglutition and generalized pains. In a few who have agranulocytosis the course is characterized by fever, pain over the splenic region, and splenic enlargement. The splenomegaly may be slight to moderate In the less severe instances there may be no symptoms

EXAMINATION. There is a general pallor though the mucous membranes are of normal color or cyanotic. Dermatitis and cutaneous rashes are common. Jaundice without enlargement of the liver is often present. A cervical adenopathy is common Gangrenous ulceration may be found on the gums, tonsils, soft palate, lips, pharynx or buccal mucous membranes, and in the nose, vagina, uterus, anus and rectum Splenomegaly and bone tenderness are usually observed The fever is high, the pulse rapid and weak, and death may ensue in from 3 to 9 days

In allergic agranulocytosis not only the granulocytes but also all other types of leukocytes are reduced in number In fulminating cases the leukocyte count may be less than 2,000 per cubic millimeter of blood and frequently it is less than 1,000

The majority of the cells are lymphocytes In some cases monocytes may be increased relatively and in absolute numbers. In chronic or recurrent types the leukocyte count is rarely less than 2,000 cells per cubic millimeter and the granulocytopenia is less pronounced Usually there is no anemia or thrombocytopenia The sedimentation rate, however, is greatly accelerated

The bone marrow shows normal erythropoietic tissues and normal numbers of megakaryocytes but no granulocytes Plasma cells, lymphocytes and reticulum cells may be increased in number

DIAGNOSIS The diagnosis is based on the presence of the agranulocytopenia The various types of pharyngitis and other infections occurring in the mouth or throat are accompanied by leukocytosis.

Sulfonamides and penicillin have improved the prognosis in this condition by control of the infection until the bone marrow can recover The mortality rate may be more than 50 per cent

Death may occur as the result of hemorrhage following necrosis of mucous membranes or from other causes, even after hematologic improvement seems assured.

Improvement is made certain by the reappearance of leukocytes of the granular series in the blood

Leukemia. Figuratively speaking, leukemia is a malignancy involving one of the series of leukocytes of the blood. There are both acute and chronic forms of leukemia. The acute and the chronic forms are subdivided by the hematologist according to the predominating type of leukocyte and by the clinician according to the rapidity of the progress of the disease. Myelogenous (myeloid) and lymphogenous (lymphatic, lymphoid) forms are distinguished Myeloid leukemia may be referred to as myelogenous, myelocytic, or histiocytic.

Eosinophilic leukemia, polymorphonuclear (neutrophilic) leukemia and basophilic leukemia are names applied to those rare instances in which these cells predominate Monocytic and megakaryocytic leukemias are so diagnosed by the hematologists.

Aleukemic leukemia is the common term used in referring to cases of leukemia in which there is no leukocytosis By some this condition is termed subleukemia

Chronic myelocytic leukemia seems to be commoner in younger persons than the chronic lymphocytic form which is more liable to occur in aging men

Chloroma, derived from the color of the tissue-forming tumors, designates tumors which may occur in the leukemic state. The term may be applied to the disease also.

The etiology is not known Leukemia has occurred frequently enough in several members of a family to give credence to the belief that often there is a hereditary etiologic factor, especially in the lymphocytic form

Congenital myelogenous leukemia is recorded Leukemia occurs oftener in the first 5 years of life than in other periods and here too it is frequently the acute myelogenous form. The disease is commoner in males than in females

An analysis, by Cooke, of the sex and age incidence in 1,500 cases of acute leukemia in children showed the following trends (1) During childhood there is a gradual increase in the proportion of males over females who have acute leukemia, the predominance of boys being greater in later childhood than during infancy. In the first year of life the disease was observed in girls oftener than in boys (2) The age incidence follows a regular curve, which rises from a moderate elevation in the first two years of life to a peak of highest incidence in the third and fourth years, with a sharp decline in the next 3 years and a more gradual progressive fall throughout the latter half of childhood Cooke concluded that acute infections form one of the factors in the production of the disease and therefore play an important part in its causation, since (1) the highest incidence in acute leukemia occurs in early childhood, (2) the type of its age incidence curve tends to follow the frequency of acute infections in children and (3) some acute infection frequently precedes the development of acute leukemia.

After the age of 50 years chronic lymphocytic leukemia is more frequently encountered than the myelogenous types of the disease After the first year of life, the disease is commoner in males than in females

In summary, the etiologic factors present in leukemia, whether they are extrinsic intrinsic or genetic are of unknown origin These [illegible]

cell growth and maturity, much as cancer cells grow.

The *clinical manifestations* of leukemia appear in acute and in chronic stages The disease does not originate in an acute form which progresses to the chronic stages The chronic forms are dissimilar in cellular morphology and are often insidious in onset However, a chronic leukemia will manifest an acute exacerbation of cellular growth and symptoms.

Acute Leukemia. The first symptom of acute leukemia is often the rapid development of weakness and pallor There may be bleeding from the mucous membranes, petechiae and ecchymoses in the skin, sore throat, cough, dyspnea, and generalized pains The pains may be limited to the abdomen The fever, headache, and prostration may be as great as those of some severe infections

A generalized pallor of the skin is characteristically present Often in acute leukemia there is an absence of lymph-node enlargement. In other instances of the disease cervical lymph-node enlargement is great. Generalized adenopathy is more frequently present in lymphoblastic leukemia than in myelogenous leukemia

Purpuric manifestations are characteristically present on the mucous membranes in the nose and the oral cavity. Partially clotted blood may be found at the gingival margins of the teeth, and the gums themselves may be swollen and purplish, the

swelling is sometimes so great that the gums may be pushed over the teeth. Slight trauma on the swollen gums often will leave a hemorrhagic area. Purpuric manifestations, blisters and ecchymosis may be present over any of the areas of glabrous skin.

Splenomegaly is not demonstrable in all cases of acute myelogenous leukemia. However, there is always some enlargement of the spleen in this disease. Splenomegaly may be absent in acute lymphatic leukemia.

Infiltration may occur in the larynx causing hoarseness A mediastinal mass may be the first sign of acute leukemia Effusion into the pleural cavities may be present as a late manifestation

Leukemic nodules have been found in the rectum, appendix, and cecum. The liver often is enlarged The rectal nodules may appear as hemorrhagic polyps and result in profuse rectal bleeding

There may be hematuria, pain and, often, priapism which is exquisitely painful and resists all forms of treatment

Hemorrhage may be present in the conjunctivae, eyelids and other parts of the eyes Exophthalmos is characteristic of chloroma Hemorrhages in the oculi fundi are variable in size and consist of pale centers with red borders Deafness may occur as the result of hemorrhage into or infiltration of the labyrinth or the auditory nerve.

Cranial nerve palsies affecting the oculomotor, facial, and trigeminal nerves, and hemiplegia and other forms of paralysis, convulsions, and findings suggesting encephalitis, meningitis, and transverse myelitis may be present There may be failure of vision, deafness and anosmia from injury from hemorrhages affecting the optic, auditory and olfactory nerves

Anemia and thrombocytopenia of some degree are present in every case of acute leukemia. The anemia is usually normocytic.

Thrombocytopenia is characteristic of acute leukemia Bleeding time is prolonged, clot retraction is poor and the result of the tourniquet test is positive

The leukocyte count is rarely high and may be normal or subnormal It may be as low as 400 per cubic millimeter of blood Persistent leukopenia, together with anemia and thrombocytopenia, often is found to be leukemia The number of leukocytes then suddenly rises to counts as high as 100,000 per cubic millimeter.

There is a distinct predominance of immature leukocytes not usually found in the circulating blood It is by the predominating type of leukocytes that acute leukemia is recognized during life When there is leukopenia, it is these immature cells which are predominant in the bone marrow and which increase in number as the leukocyte count rises

In *acute myeloblastic leukemia* the immature leukocytes possess the characteristics of myeloblasts and undifferentiated myelocytes The presence of immature cells which possess a few granules suggests that the associated cells devoid of granules are of the myeloid series The granules can often be demonstrated in peroxidase stains

The presence of many myelocytes or a large spleen and the lack of hemorrhagic phenomena and thrombocytopenia suggest the chronic form of the disease.

In *acute lymphoblastic leukemia*, the predominant cells (lymphoblasts) make up about one half of the total number of cells The remainder of the cells are recognizable lymphocytes, some of which contain a few azurophilic granules A few neutrophilic leukocytes and perhaps an occasional myelocyte may be reported

Monocytic leukemia is recognized by the presence of large numbers of cells which can be definitely identified as monocytes.

The monocytes represent a separate series of cells and for this reason monocytic leukemia is separated from myelogenous and lymphatic forms of the disease. Reminiscent of former beliefs in regard to the origin of the monocyte and thus of the

different terminologies are the terms monocytic leukemia of the Naegeli type or monocytic leukemia of the Schilling type. The monocytic leukemia of the Naegeli

Proliferation and transitions to the freely circulating monocytic cells appear to depend on the age of the patient and the degree of stimulation A fulminating course in a young person will produce extensive reticulum hyperplasia because the maturation of the cells cannot keep pace with proliferation. In an older person a similarly acute course will produce less hyperplasia because the tissues are less adaptable to proliferation A heterogeneous accumulation of leukocytic elements, producing findings resembling those in Hodgkin's disease, may be present in acute instances. The brain may contain leukemic infiltrates and hemorrhages which are a contributory or an immediate cause of death.

Monocytic leukemia occurs more frequently in men between 40 and 60 years of age, although no age or sex is exempt.

The manifestations are those common to other acute and chronic forms of leukemia Necrotic ulcerations in the buccal cavity and pharynx, diversity and severity of skin lesions, attended by severe pain are the only manifestations observed more commonly in monocytic leukemia than in other forms of the disease.

The diagnosis is made by recognition of the immature monocytes in the stained blood smears In some instances it may be necessary to make histologic studies

In rare instances a monocytic leukemia is manifested as a chronic leukemia.

In rare instances acute or subacute *eosinophilic, basophilic* or mast cell, *neutrophilic,* and *plasma cell* leukemias may be observed In each of these leukemias the type of cell present is the only distinguishing feature.

Leukosarcoma refers to an acute leukemia characterized by the presence of the blood findings of an acute leukemia in a patient known to have lymphosarcoma (Hodgkin's disease).

By the time the patient is aware of a definite illness, the symptoms are those resulting from anemia, or the pressure of an enlarged spleen or liver, enlarged lymph nodes, or leukemic infiltrations in various organs and tissues Pain, limitation of movement, and other symptoms which suggest arthritis, osteomyelitis, or rheumatic fever are rare but when present may be due to pathologic fracture of bone which may occur in either acute or chronic leukemia Fractures are commoner in children who have acute myelocytic leukemia than in those who have chronic leukemia Sternal tenderness occurs in leukemia, but this is most commonly due to an associated esophagitis or peptic ulcer

Symptoms may arise as the result of compression by bony tumors on nerves or other structures A single bone tumor in chronic myelocytic leukemia is rare. These bone tumors are usually multiple Periosteal stripping, foci of bone destruction, and areas of osteoporosis occur and may cause bone pain Leukemic proliferation in the juxta-articular portions of the bone may give rise to symptoms resembling those of an acute arthritis

Many of these patients have symptoms attributable to the increased metabolic rate such as loss of weight, nervousness and abnormal perspiration As the disease progresses, cachexia is inevitable A few patients have chronic hemoptysis, or rectal bleeding and fever.

The abdominal symptoms in lymphocytic leukemia may appear at any time or late in the course of the disease In a small proportion of cases the first symptom may

be abdominal pain, continuous or intermittent, symptoms of intestinal obstruction; abdominal tumor or serious gastrointestinal hemorrhage.

On examination the patient may have a normally colored skin and appear healthy Some are pale and tired in appearance and show evidence of loss of weight Extreme enlargement of the spleen may be evident on inspection. The spleen is almost always palpable in all forms of chronic leukemia.

Lymph-node enlargement is uncommon early in myelocytic leukemia. As the disease advances, slight or very moderate enlargement is found. Lymphocytic leukemia contrasts sharply in this respect, for lymph-node enlargement appears early and may be extensive, involving all nodes The nodes are discrete, firm, and freely movable without tenderness

Cutaneous lesions may be the first symptoms of leukemia, the blood changes and other changes appearing later, or they may make their appearance at any time during the course of the disease The cutaneous lesions (leukemids) may resemble a nonspecific lesion which may be found in other conditions. The leukemids include vesicles, pustules, wheals, bullae, petechiae, hematomas, papules, nodules, herpes zoster and prurigo lymphatica Pigmentary changes may be present as well as sensory disturbances such as itching and burning The specific lesions for leukemia consisting of leukemic cells like leukemids are difficult of identification, except on biopsy Bleeding into the skin is common in acute leukemia and may occur in the late stages of chronic leukemia, especially in lymphocytic leukemia.

Herpes zoster may occur in leukemia and in rare instances may be followed by paralysis.

An erythroderma occurs in chronic lymphocytic leukemia which is characterized by progressive reddening of the skin, together with thickening and edema or thinning and atrophy The cutaneous involvement may be diffuse and generalized, and when the skin of the whole body is involved, the condition is the so-called universal leukemia cutis Localized erythroderma rarely occurs anywhere except on the face The lesions may be yellowish brown, red, bluish red or purplish, and they may be nodular. Ulceration and necrosis rarely ensue

Lesions of the skin are rare in *chronic myelocytic leukemia.* When skin lesions do occur they are described as firm, circumscribed, brownish, gray or bluish cutaneous and subcutaneous nodules varying in size, measured in millimeters to several centimeters The appearance of leukemic nodules in the skin in myelocytic leukemia is of immediate, grave prognostic import

In chronic lymphocytic leukemia enlargement of the tonsils may be a relatively early finding and may reach extreme proportions Enlargement of the tonsils in an elderly person should be considered as either leukemia or malignant disease until proved otherwise Very rarely the breasts or the salivary and lacrimal glands may be involved and present symmetric painless enlargements (Mikulicz's syndrome)

Exophthalmos is characteristic in chloroma It may be of unequal degree in the two eyes. Examination of the fundus reveals engorgement of veins, hemorrhages, exudates and blurring of the disk Infiltration by leukocytes may appear as white lines sheathing the peripheral portions of veins Often the ophthalmologist can suggest the diagnosis.

Occasionally in chronic myelocytic leukemia sudden blindness due to hemorrhage may occur in one eye Leukemic infiltrations may involve the iris, cornea, and sclera

Hemorrhage or infiltration in the external, middle or internal ear, or infiltrations along the course of the eighth nerve may produce deafness, otitis media or Ménière's syndrome.

Cough may be present and fine crepitant rales are often heard over the bases of the lungs. There may be atelectasis, mediastinal tumor from lymph node enlarge-

ment, or pulmonary infiltration or pleural effusion Such changes are much less frequent in the myelocytic form (see Mediastinal Tumors, Chapter 9).

Enlargement of the heart, systolic murmurs, tachycardia and edema are common findings Infiltrations in the myocardium are common, but myocardial failure attributable to leukemia is rare and the diagnosis cannot be made during life

In those who have had severe abdominal pain, manifestations of intestinal obstruction or hemorrhage may be responsible for the pain. On examination by the roentgenologist or the surgeon gross deformities are not present. The symptoms arise from an extensive cellular (lymphocytic) infiltration of the intestines. Consequently the term *pseudoleukemia gastrointestinalis* has been employed to designate these cases. In the stomach pseudoleukemia gastrointestinalis may closely resemble carcinoma

The liver is often enlarged. Jaundice and ascites are unusual.

In chronic myelocytic leukemia 9 of every 10 patients have enlargement of the spleen at the first examination. The spleen is smooth and hard and the notches in the border are easily felt The spleen may be extremely enlarged, and it may extend to the ilium laterally and around to the right anterior superior spine.

In chronic lymphocytic leukemia the spleen is not so large as in myelocytic leukemia It may extend only one or more fingerbreadths below the costal margin. It is very rare in chronic leukemia that neither the spleen nor the lymph nodes are enlarged but such lack of enlargement has been observed

The splenomegaly is painless and the spleen is nontender unless infarcts and perisplenitis are present and give rise to a degree of pain and tenderness as to suggest the presence of some abdominal emergency. A friction rub may be felt and heard over the spleen after infarction

Any part of the nervous system may be involved in leukemia, and the findings on physical examination are thus of wide range since they are produced by hemorrhage, thrombosis, infiltration with leukemic cells, or tumor-like masses

In *chronic myelocytic leukemia,* well-marked leukocytosis is the rule. A count of 30,000 to 40,000 is frequently found at the time the disease is first discovered. Lower counts may be encountered, even if the symptoms and the degree of anemia indicate far-advanced disease In some instances the count may be normal or low, as in aleukemic leukemia

The segmented neutrophils comprise most of the leukocytes. Metamyelocytes and myelocytes are found in great numbers Only a few undifferentiated myelocytes and only a small number of myeloblasts are found in chronic myelocytic leukemia Eosinophilic and basophilic myelocytes are increased sufficiently to maintain or exceed their normal numerical ratio The percentage of lymphocytes is relatively low.

In *chronic lymphocytic leukemia* the total leukocyte increase is seldom as great as in leukemia of the myelocytic type, the average being between 25,000 and 35,000 per cubic millimeter and comprised mainly of small lymphocytes Large lymphocytes not infrequently are found Immature lymphocytes occur less commonly.

Sternal aspiration is not performed as a diagnostic test in leukemia except when the diagnosis is in question

Chronic Megakaryocytic Myelosis. The syndrome of chronic splenomegaly —weakness, leukemoid peripheral blood findings and myelofibrosis with osteosclerosis—is described under a variety of terms. These include chronic nonleukemic myelosis, myeloid megakaryocytic hepatosplenomegaly, megakaryocytic nonleukemic myelosis and agnogenic myeloid metaplasia of the spleen

The liver and the spleen are greatly enlarged The sinusoids of the liver contain giant cells of megakaryocytic characteristics The basic splenic architecture may be

unaltered, but the extrafollicular parenchyma is filled with myeloid metaplasia containing megakaryocytes. The reticulum of the lymphatic sinusoids may contain large numbers of megakaryocytes. The bones are sclerotic. The megakaryocyte is regarded as the *sine qua non* of this chronic myelosis. The two forms of giant cells, megakaryocytes and Sternberg-Reed cells, are easily confused.

The symptoms and physical findings may resemble those of Hodgkin's disease with pulmonary involvement There may be dyspnea and cyanosis and wheezy expiratory rales The abdomen may be distended by the enlargement of spleen and liver Ricker has expressed the opinion that the process is probably malignant, an indolent myelogenous leukemia.

Aleukemic or Subleukemic Leukemia (*Leukopenic Myelosis*). The clinical features of leukemia without leukocytosis are similar to those of leukemia with leukocytosis Acute and chronic forms are encountered, and myelogenous, lymphogenous and monocytic types have been described The recognition of subleukemic leukemia is often difficult. The study of the sternal marrow is helpful

Chloroleukemia (*Chloroma*) Chloroma is usually of myelocytic origin However, a case of monocytic chloroma has been described The characteristic tumefactions are situated in relation to the periosteum and ligamentous structures of the skull, paranasal sinuses, orbits, spinal column, ribs and sacrum These tumefactions are observed more commonly in children and young adults than in older persons The general clinical manifestations simulate those of acute leukemia. The blood changes are indistinguishable Chloroma may cause protrusion of the eyeball, with diplopia and loss of vision, pain, deafness, and other cranial nerve palsies. Inside the skull or extending into the skull, chloroma causes the symptoms of pressure, infiltrative growths, or expanding tumors

A patient who has chronic leukemia may remain comfortable for years with cell counts of more than 100,000 cells

DIAGNOSIS OF THE LEUKEMIAS

The combination of glandular enlargement, splenomegaly, leukocytosis consisting mainly of immature leukocytes, and anemia is unmistakable

The immaturity of the leukocytes is of greater significance than the leukocyte count *itself*

Thrombocytopenia, with prolonged bleeding time, poor clot retraction and positive reaction to the tourniquet test, is an almost invariable accompaniment of acute leukemia

Aleukemic leukemia should be suspected whenever there are splenomegaly, lymphadenopathy, fever, purpura or retinal hemorrhages, swelling of the gums, deep bone pains, bone tenderness, pathologic fractures and bone tumors It is in these patients that sternal puncture has its most valuable application in leukemia.

The average duration of life following the onset of symptoms is between 3 and 4 years irrespective of treatment

ERYTHROCYTES (NORMAL AND PATHOLOGIC)

The erythrocytes are formed mainly from the sinusoids of the bone marrow but some arise from the spleen, lymph nodes, liver, suprarenal glands, cartilage, adipose and other tissues These cells are non-nucleated, round, inert bodies measuring on the average 7.2 to 7.9 microns in diameter. The erythrocyte is about two thirds water and about one third hemoglobin The hemoglobin is about two thirds protein and the rest is lipids and *inorganic salts*

The erythrocyte remains useful for about 120 days. A volume of packed cells equaling about 50 ml is destroyed daily, the fragments of these cells are phagocytized by the reticuloendothelial system The hemoglobin is changed to bilirubin, urobilinogen and urobilin for excretion in the feces and the urine

The erythrocyte contains no definite cell membrane though capable of withstanding much trauma during its circulation through the vascular system. Whether or not there is an outer cellular membrane, in the presence of hypotonic and hypertonic sodium chloride solutions the cell behaves as though there were a membrane.

The main function of the erythrocyte is to transport oxygen from the pulmonary capillaries to the tissues and to bring back carbon dioxide to be liberated by the lungs These mechanisms are described at length and in detail by both chemists and physiologists

The mechanism which regulates the number of erythrocytes in the normal circulating blood is not known At present all hypotheses are undergoing reconsideration in regard to the role of the vitamin B group (especially B_{12}) in erythropoiesis. Iron is necessary for hemoglobin formation, and it seems that copper too, as a catalytic agent, is essential to the process Protein is likewise necessary; hematopoiesis continues, however, when the protein intake is very low.

The stages of development of erythrocytes are designated by a variable terminology. Irrespective of stages of development it is well to consider the *megaloblast* to be the earliest form of erythrocyte which is recognized It is a large cell (12 to 18 microns in diameter) with a centrally placed round nucleus

The *erythroblast* is considerably smaller than the megaloblast and is the first of the series to contain hemoglobin in its cytoplasm

The *normoblast* is the usual nucleated erythrocyte observed in smears of peripheral blood.

The *erythrocyte* is the mature red blood cell It is a circular biconcave disk 6 to 9 microns in diameter and 1 micron thick

The following terms are used in description of erythrocytes Anisocytosis designates variations in size A microcyte is less than 6 microns in diameter. A macrocyte is greater than 10 microns in diameter. Poikilocytosis implies variations in shapes of erythrocytes. Variations in the staining properties of these cells are termed achromia, hypochromia, hyperchromia, polychromatophilia and punctate basophilia or polychromasia.

Variations in structure are implied by the employment of the following terms: Cabot's rings, Howell-Jolly bodies, reticulocytes and nucleated erythrocytes. Hematologists employ certain other terms in description of the variations in structure of the erythrocytes. a target cell is an erythrocyte which resembles a target used on a rifle range—a dark central zone, a light ring, and then a deeply stained outer rim Oval-shaped cells characterize ovalocytosis, a rare hereditary condition without known significance in white and colored races Spherocytes are erythrocytes that have lost their biconcave shape These cells characterize familial and acquired hemolytic icterus.

Variations in staining reactions are designated by the term basophilia or polychromasia. Romanowsky-stained preparations of blood reveal a limited number of erythrocytes which have been tinted a diffuse bluish color (Howell-Jolly bodies). This cellular reaction is termed basophilia. The term punctate basophilia or stippling is applied to erythrocytes showing discrete, bluish black granules after staining

Reticulocytes are made evident by vital staining technic and comprise from 0.2 to 0 8 per cent of the erythrocytes of normal blood. *Reticulocytes in increased numbers* are constant and dependable evidence of active regeneration It is believed that they disappear within a few days as the cells mature in the circulation. A sudden increase of these cells in the blood is termed a reticulocyte crisis. Such a crisis may occur within a few days after the institution of effective treatment in severe instances of pernicious anemia or after hemorrhages Reticulocytes are especially numerous in familial hemolytic jaundice.

Nucleated erythrocytes or normoblasts are approximately the size of a normal erythrocyte. The more nearly mature forms contain a nucleus which has a diameter less than two thirds of that of the erythrocytes It is round, and stains a dense, homogeneous, purplish black color without showing any structure (pyknotic). The cytoplasm may be normal or basophilic or may vary in degree of reaction to stains

The more primitive erythroblasts, which are present in some severe anemias, have nuclei and nucleoli The cytoplasm is abundant and is strongly basophilic.

Megaloblasts or *promegaloblasts* are the primitive cells of the erythrocytic series. These cells rarely if ever occur in the blood except in severe untreated pernicious anemia

Nuclear particles of the erythrocytic series differ from granules. When they are in the form of coarse granules, they are called Howell-Jolly bodies. They may also occur as filaments which are variously looped or curled (Cabot's rings). These may be present in any condition in which nucleated erythrocytes are present, and have about the same significance

ERYTHROCYTE COUNT. The erythrocyte count in newborn infants is about 5,500,000 per cubic millimeter of blood It falls rapidly during the first few weeks to about 5,000,000, and reaches a minimum (about 4,500,000) at one year During childhood it is somewhat lower than during adult life. In adult men it is about 5,500,000, in adult women, about 4,500,000 to 5,000,000 per cubic millimeter. The erythrocyte count fluctuates with changes in plasma volume, or with the storage of red cells in, or their release from, the spleen and other reservoirs. These fluctuations in values rarely exceed the fluctuations in the numbers of erythrocytes from error in counting.

In the clinical practice of medicine the average normal values for numbers of erythrocytes as reported from the laboratory are about half a million less than the foregoing values.

ERYTHROCYTOSIS. An erythrocytosis (polycythemia) signifies an increase above the normal in the number of erythrocytes in the circulating blood A transient erythrocytosis is present in the newborn infant and in adults during short exposures to high altitudes These increases are transient and are comparable to leukocytosis An erythrocytosis is due to the effect of anoxemia on the bone marrow which may stimulate excessive production of erythrocytes by some by-product of asphyxia. Commonly the anoxemia of erythrocytosis is due to impaired pulmonary ventilation, decreased atmospheric pressure, defective pulmonary circulation, or a reduction in the oxygen-carrying power of the hemoglobin. The usual causes for reduction of the oxygen-carrying power of the hemoglobin are the effects of various chemical agents and drugs with special reference to the coal-tar derivative aniline and its derivatives, phosphorus and cobalt.

ERYTHREMIA An erythremia denotes an absolute increase in the number of circulating erythrocytes due to an excessive production by the bone marrow (absolute polycythemia). The cause for this excessive production is unknown, and therefore erythremia is analogous to leukemia

HEMATOCRIT (VOLUME OF PACKED CELLS). The volume of packed cells obtained by centrifugation of whole blood is termed the hematocrit The average normal value of packed cells for men is 45 ml per 100 ml of blood, for women it is 42 ml.

ERYTHROCYTIC INDEXES (WINTROBE). There are certain indexes of the erythrocytes which are often used and referred to in the diagnosis of diseases and conditions involving the erythrocytes.

The *color index* is the quotient of the percentage of hemoglobin divided by the product of the first two figures of the erythrocyte count by two The normal index is 1

The *volume index* is the product of the number of *milliliters of packed* cells per 100 ml (the normal mean volume of packed cells is 43 2 ml per 100 ml of blood) and 2.3 divided by the product of the red cell count (millions per cubic millimeter) and 20

The [illegible] of packed

cells per

Normal [illegible]

The *saturation index* is the quotient obtained by division of the percentage [illegible] number of milliliters of packed erythrocytes per 100 ml

[illegible] he normal range is from 0 9 to 1 2

[illegible] is the quotient obtained by dividing the hemoglobin [illegible] by the number of erythrocytes in millions per cubic millimeter. The results are in micromicrograms

The normal range of values for adults is 29 (± 2) and for children, 26 to 28

Mean corpuscular hemoglobin concentration is the quotient obtained by division of 100 times the hemoglobin in grams per 100 ml. of blood by the volume of packed corpuscles in milliliters per 100 ml. The normal range for children is 32 to 34, for adults 34 (± 2).

OXYGEN-COMBINING POWER The blood of the normal young man has an average oxygen-combining capacity of 20 9 volumes per cent, corresponding to 15 6 gm. hemoglobin per 100 ml (Van Slyke). This value for the oxygen-combining power is too high for the average patient In practice 14 to 14.5 gm. of hemoglobin is to be considered the usual upper limit of the normal value.

HEMOGLOBIN. Hemoglobin is a conjugated protein consisting of iron in combination with protoporphyrin and globin It is found in the bone marrow and within the erythrocytes Hemoglobin forms an unstable compound with oxygen and on exposure to air in the lungs forms oxyhemoglobin, which enables it to carry oxygen to the tissues. In the tissues the oxygen is lost from the hemoglobin, and reduced hemoglobin is formed by the addition of carbon dioxide which is then transported to the lungs and exhaled

Hemoglobinometers are of three general types. (1) those based on direct matching of the unchanged blood with color scales (Tallqvist and Dare); (2) those based on the conversion of hemoglobin into acid hematin (heme) with matching colors (Sahli, Sahli-Hellige, Newcomer, Wintrobe, Haden-Hausser and Osgood-Haskins); (3) the photoelectric-cell method of Exton and Sheard-Sanford.

The American Society of Clinical Pathologists has decided that hemoglobin should be reported in terms of grams per 100 ml of blood The calculation takes into account the age and sex of the patient According to Wintrobe the average normal values in grams per 100 ml of blood from birth to adult age are as follows First day 19.5 ± 5, two to eight days 18 3 to 19 0 ± 4, two to eight weeks 14 0 ± 3 3, three to eleven months 11.8 to 12 2 ± 2.3, one to two years 11 2 to 11.8, three to ten years 12.5 to 12 9, eleven to fifteen years 13 4, adult males 16 0 ± 2 In practice it is the exception, not the rule, to find men who have a hemoglobin of 14 0 gm. or more Women have less.

Postprandial Variation in Hemoglobin. Branwood showed that the percentage of hemoglobin in the peripheral blood has a postprandial decrease of the order of 5 to 10 per cent This fall is in proportion to the size of the meal—the larger the meal the greater the fall There is also, presumably, a fall in the number of erythrocytes at this time This decrease in hemoglobin is probably due to a redistribution of the cells from the periphery to the abdominal viscera and possibly also to slight changes in blood volume This fall in hemoglobin can be prevented by exercise or by the administration of epinephrine Patients who have hypertension and hyperthyroidism do not share this postprandial decrease in hemoglobin.

Hyperchromia is an increase in the total amount of hemoglobin whereas oligochromia designates a decrease

BLOOD IRON The absorption and utilization of iron in the human organism are of interest and importance because of the frequent therapeutic need for this element. The importance of hydrochloric acid and ascorbic acid (vitamin C) in the release and the reduction of iron to the ferrous state in the stomach of human subjects is certain Protein digestion products also appear somewhat effective in the release of iron Hence, ascorbic acid and dietary protein may actually increase the availability of food iron

It has been demonstrated that the beta fraction of the serum globulins transports the serum iron In cases of iron deficiency anemia the serum iron value is much less than normal (normal values 0 08 to 0 17 mg per 100 ml). The iron-binding globulin is only about 9 per cent saturated The degree of saturation in hemochromatosis and transfusion hemosiderosis is nearly 100 per cent

Little or no iron is excreted in the urine and only small amounts are eliminated in the feces, probably by way of the bile This concept visualizes the human organism as a tight compartment, as far as iron is concerned, and further implies that little or no absorption of exogenous iron into the closed space occurs other than to replace blood

loss A significant amount of iron may be excreted in human sweat by the normal adult male subject.

In vitro studies, in which radioactive iron (as Fe^{59} or Fe^{55}) is used as a tracer, present convincing evidence that heme synthesis occurs in the immature erythrocyte itself. The rate of iron uptake is greatest in the normoblast, but even the reticulocyte shows a definite uptake. The radioactive iron is present in the recrystallized heme obtained from the hemoglobin of these cells Addition of either folic acid or liver extract to the immature erythrocyte increases the rate of heme synthesis, as manifested by an increased rate of iron uptake.

The normal iron content of the blood is 40 to 60 mg. per 100 ml, averaging about 52 mg. in males and 45 mg in females Practically all of this is in the red blood cells in the form of hemoglobin (15.6 gm. per cent). The inorganic iron content of whole blood averages only about 1 to 1 7 mg. per 100 ml There is a small amount of inorganic iron in the plasma or serum, 0 08 to 0 17 mg per 100 ml This value is rather constant in the fasting state and is probably an index of the activity of the intermediary metabolism of iron, particularly destruction and production of hemoglobin About 90 mg of iron is liberated daily by normal breakdown of erythrocytes

After ingestion of *inorganic iron salts*, the plasma iron concentration rises to maximal levels of about three to four times the fasting level in about 2 to 4 hours, subsequently declining gradually over a period of 6 to 12 hours, depending on the dosage Thus the plasma appears to be the medium of transportation of iron from the intestinal tract to the tissues in which it is further utilized or stored Absorbed iron is transferred to the erythrocytes with remarkable rapidity, as has been demonstrated by radioactive iron.

The *plasma iron* is influenced by and may be regarded as a measure of the quantity of iron absorbed from the intestine, the adequacy of the iron reserves of the tissues, the capacity of the bone marrow to utilize iron in hemoglobin synthesis, and the activity of hemolytic processes

Disturbances in the metabolism of iron are evidenced by a decreased hemoglobin formation, decrease in circulating hemoglobin, or abnormal deposition of iron-containing pigment in the tissues (hemosiderin) Certain forms of hypochromic and microcytic *anemia* are dependent on inadequate supply or absorption of iron.

Iron deficiency may also occur as a result of *hemorrhage*, with consequent exhaustion of the available tissue reserves of this element. Low values for plasma or serum iron have been reported in hemorrhagic and hypochromic types of anemia High values are present in forms of anemia, such as pernicious anemia, characterized by diminished hemoglobin formation not due to iron deficiency

Deposition of excessive amounts of iron-containing pigment (hemosiderin) in the tissues occurs as a result of excessive breakdown of erythrocytes in hemolytic types of anemia, in conditions in which hemoglobin synthesis is inadequate owing to factors other than iron deficiency (pernicious anemia), and in hemochromatosis, the cause of which is unknown. In the latter condition enormous amounts of iron may be deposited in the tissues, particularly in the liver, pancreas and retroperitoneal lymph nodes

Hemoglobinuria. Paroxysmal Cold Hemoglobinuria. In the syndrome of paroxysmal cold hemoglobinuria the intravascular hemolytic reaction is dependent on the presence in the serum or plasma of a hemolysin, which is absorbed by the erythrocytes only at low temperatures Complement is not necessary for this phase but is essential for hemolysis to occur when the body is rewarmed (the Donath-Landsteiner reaction) The serum of patients who have paroxysmal cold hemoglobinuria will hemolyze the red blood cells of other persons in the same blood group, but the erythrocytes of patients with this condition are not lysed by the serum of normal persons. This hemolysin is distinct from the Wassermann reacting substance (that is, reagin), and there is no correlation between the titer of the complement fixation or flocculation tests for syphilis and that of the hemolysin, except that both usually decrease following antisyphilitic therapy.

Evidence that this disease is caused by syphilis seems well established, but the mechanism remains obscure. The coexistence of active clinical syphilis and paroxysmal cold hemoglobinuria is uncommon This condition occurs in latent syphilis or occasionally in dementia paralytica. The finding of the Donath-Landsteiner hemolysin in patients with late syphilis has varied from less than 0 2 per cent to 20 per cent. In a study by Donath and Landsteiner of 93 patients who had dementia paralytica, only 1 patient was found to have paroxysmal cold hemoglobinuria, but 6 others had a positive Donath-Landsteiner reaction without clinical manifestations of hemoglobinuria

SYMPTOMS After exposure to cold the patient soon experiences muscular aches and pains, abdominal cramps, headaches, nausea and vomiting Certain patients manifest vasomotor disturbances such as urticaria, or Raynaud's phenomenon may occur. Shortly after exposure to cold the patient experiences a shaking chill, the severity of which is dependent on the degree of hemolysis. The patient's temperature may rise to 102 or 104 F (38.3 or 40 C) If large numbers of erythrocytes are hemolyzed, the patient may be definitely jaundiced.

On examination the patient is weak and the blood pressure may be low. The liver and the spleen are occasionally palpable during the attack

One to four hours after chilling, the urine becomes dark red, wine or mahogany in color It frequently contains albumin, casts and even a few erythrocytes. Spectroscopic examination reveals that the color is due to oxyhemoglobin, methemoglobin and sometimes hematin The erythrocyte count and hemoglobin content may drop decidedly after an attack An initial neutropenia occurs during the exposure to cold, followed by leukocytosis in the chill phase. The blood serum is colored pink, and in severe instances the serum bilirubin may be elevated. Reaction to the serologic test for syphilis is almost always positive If the patient gives persistently negative reactions to tests for syphilis, the diagnosis of paroxysmal cold hemoglobinuria should be questioned

The majority of patients who have paroxysmal cold hemoglobinuria usually manifest *a positive response to Ehrlich's test This test consists of binding the finger with a liga*ture and immersing it in ice water for a few minutes. After the finger is warmed, local hemoglobinemia can be demonstrated This reaction is less hazardous than the reaction to the Rosenbach test and is preferable in the investigation of patients who have hemoglobinuria The *Rosenbach test* consists of immersing the hands or feet in ice water for 10 to 20 minutes The resulting hemolysis may produce severe constitutional symptoms and has occasionally resulted in anuria Repetition of the cold water test may cause sufficient depletion of the patient's complement that negative reactions are obtained

The *Mackenzie* "rough" test consists of chilling a sample of the patient's blood in ice water A positive result is denoted by hemolysis after the blood is rewarmed In the Donath-Landsteiner test a mixture of the patient's erythrocytes, varying dilutions of his serum and guinea pig complement, is immersed in ice water and then rewarmed Hemolysis of the patient's cells is a positive result. Appropriate controls are necessary for interpretation of results in these tests

DIAGNOSIS The diagnosis is based on the foregoing findings, the history of exposure to cold, and the presence of hemoglobinuria

Differentiation from other types of hemoglobinuria is usually relatively simple In the *Marchiafava-Micheli syndrome* the hemoglobinuria occurs only at night. The Donath-Landsteiner reaction is negative in both the Marchiafava-Micheli syndrome and march hemoglobinuria, but positive in cold hemoglobinuria Paroxysmal cold hemoglobinuria is differentiated from that caused by cold hemagglutinins by the finding that hemolysis occurs while there is exposure to ice water, and that rewarming is not necessary for the hemolysis

March Hemoglobinuria. Like orthostatic albuminuria, march hemoglobinuria occurs after exercise in the upright position It often affects soldiers The urine be- [illegible] and brown after the march and the color persists for several hours

afterward. The color is due to the presence of hemoglobin. For practical purposes the condition is symptomless.

Hemolytic Anemia With Paroxysmal Nocturnal Hemoglobinuria. Chronic hemolytic anemia with paroxysmal hemoglobinuria is characterized by hemolytic anemia and attacks of nocturnal hemoglobinuria. It is a rare and curious disorder, the cause of which is unknown.

Venous thrombi may be found in the systemic or portal circulation. There are hepatomegaly with central zone necrosis, moderate splenomegaly with little deviation from the normal, and marked erythropoietic hyperplasia of the bone marrow. The kidneys may be enlarged. Hemosiderosis is found but it is peculiar in distribution. Free iron pigment is present in large amounts in the kidneys (convoluted tubules and ascending loops of Henle), but only traces are found in other organs.

Men are affected somewhat more frequently than women, most often in the third decade of life The attacks of hemoglobinuria are unrelated to cold, but it may have been noticed that urine which was passed during the night, or that passed when the patient arises in the morning, is dark, whereas the day urine may appear normal Weakness and yellowish discoloration of the skin and mucous membranes may be the first and only symptoms for many years, or abdominal, lumbar or substernal pain and fever may usher in an attack of hemoglobinuria.

Examination reveals jaundice, or a bronzing and pallor of the skin The spleen and the liver are enlarged. The tongue is normal and so is the nervous system.

There is macrocytic or normocytic anemia Reticulocytosis (10 to 20 per cent), polychromatophilia, normoblasts and macroblasts are present in the stained blood smear Leukopenia and thrombocytopenia are common The van den Bergh reaction is increased and indirect Spectroscopic examination reveals free hemoglobin in the plasma.

The urine contains increased amounts of urobilinogen Hemoglobinuria may be present. The urine sediment is yellow and gives a positive iron reaction

On examination of the bone marrow, normoblastic hyperplasia is the characteristic finding.

A very simple diagnostic method is the heat resistance test, in which a test tube containing about 5 ml of blood obtained by means of a dry-air sterilized syringe is placed into an incubator for 6 to 24 hours at a temperature of 98.6 F (37 C). In cases of nocturnal hemoglobinuria, hemolysis occurs which can be seen with the naked eye.

The forementioned findings are diagnostic. Congenital chronic hemolytic anemia with nocturnal hemoglobinuria is distinguished from congenital hemolytic jaundice by the negative family history and the absence of increased fragility of the erythrocytes to hypotonic saline solutions

The failure of cold to activate hemolysins distinguishes this condition from paroxysmal hemoglobinuria e frigore The finding of malarial parasites or *Bartonella bacilliformis* will aid differentiation from blackwater fever or bartonellosis Sickle cell anemia is recognized by the finding of sickle cells in wet films

Transfusions are avoided.

Anemia. Anemia is a decrease below the average normal quantity (12 to 14 gm per 100 ml) of hemoglobin in blood This may or may not be accompanied by a decrease in the number of erythrocytes Before proceeding with further discussion of blood dyscrasias it is well to discuss the ill effects of a simple anemia since these are almost always a part of the symptomology of a blood disease.

The number of erythrocytes per cubic millimeter may be reduced by (1) blood loss or an increased blood destruction, (2) decreased blood production or (3) faulty production of cells It is on these three categories of blood depletion that the various classifications of anemias are based

The terminology used in the description of an anemia may be based on the size of the cell and its staining reactions For instance, in the vernacular of the hematologist anemias are often termed normocytic, macrocytic and microcytic.

In *normocytic anemia* there is a proportionate decrease in the number of corpuscles, the quantity of hemoglobin, and the volume of packed erythrocytes. The erythrocytes have not, on the average, been changed in size or hemoglobin content.

In *macrocytic anemia* the majority of the red corpuscles are larger than normal The volume of packed cells is greater than would be expected from the cell count. The hemoglobin content is normal in proportion to the volume of each cell but owing to size the hemoglobin content is greater than that of normal cells

In *microcytic anemia,* owing to the smallness of the erythrocytes, the volume of packed cells is less than would be expected from the erythrocyte count.

In regard to the staining reactions of the cells the term *hypochromic anemia* is often employed In hypochromic anemia there is a greater decrease in hemoglobin than in the volume of packed cells The corpuscles also are usually reduced in size, and thus the term *hypochromic microcytic anemia* may be appropriate

Symptoms of Anemia. The reduction in the oxygen-carrying power of the blood and the degree of change in total blood volume are responsible for the symptoms of anemia from any cause. In addition to these symptoms of anemia there are often other symptoms caused by the disease producing the anemia.

The adjustment to the reduced oxygen-carrying power of the blood may be so effective that an erythrocyte count of 2,000,000 cells per cubic millimeter and a hemoglobin of 6 gm per 100 ml may be borne with comfort if excessive physical exertion is not practiced However, a history will usually reveal that these patients are "symptomless" but not up to their normal standards of health. The symptoms of oxygen deprivation develop when about one half of the blood has been lost. The most prominent symptoms following the sudden loss of blood are those of shock, already discussed In elderly patients who have arteriosclerosis of the coronary arteries angina pectoris may be present

When there is *rapid destruction of blood,* the manifestations of the anemia result from the disposal of the products of blood destruction These manifestations are jaundice and hemoglobinuria, and abdominal pain

Skin and Mucous Membranes Chronic pallor of the skin and mucous membranes is due to many different causes (see Chapter 8). One of the causes of a chronic pallor is anemia A waxy, dead whiteness of the skin is present in acute loss of blood Chronic intermittent loss of blood is one cause of a distinctly sallow color. The greenish sallowness once considered pathognomonic of chlorosis is observed in both young women and young men and many of them are not anemic The lemon yellow pallor in pernicious anemia is a figment of the imagination.

Respiratory System The occurrence of respiratory symptoms in those who are anemic depends on the rapidity of the production of anemia, its severity, and the reserve capacity of the cardiovascular system A rapidly developing anemia is attended by breathlessness, tachycardia and pallor

Heart In direct proportion to the reduction of hemoglobin there are palpitation, tachycardia and breathlessness on exertion. The blood pressure may be slightly lowered but the pulse pressure is high In severe anemia the blood is carrying sufficient oxygen to supply the tissues while the patient is at rest, but on exertion dyspnea is evident In more severe anemia, dyspnea may occur while the patient is at rest

Cardiac dilatation may occur in severe degrees of anemia, bringing on a functional insufficiency of the mitral and tricuspid valves and, in rare instances, of the aortic valve also In severe anemia of any type the circulatory rate is increased, with elevation of pulse pressure, stroke volume, minute volume, cardiac rate and output, and oxygen consumption, and with a decrease in the arm-to-tongue circulation time. When the hemoglobin content is less than 3 5 gm., congestive heart failure may ensue even in the absence of pre-existing heart disease Heart failure does not leave any permanent damage if the anemia is quickly and effectively treated.

In some instances of severe anemia, angina pectoris may supervene in the

absence of manifest coronary artery disease. The angina pectoris, like congestive failure, clears on adequate treatment for the anemia

A severe degree of anemia appearing in a patient who has organic heart disease causes an accentuation of the existing symptoms, or if no symptoms are present, may cause symptoms to appear

A severe anemia is accompanied by dependent edema.

Electrocardiographic abnormalities are common in severe anemia. The abnormalities consist of flattening or inversion of the T waves, depression of the S-T segments, and a tendency to low voltage of the QRS waves. With correction of the anemia the electrocardiogram usually returns to normal

The Quantity of Red Blood Corpuscles in Heart Failure. The quantity of erythrocytes labeled by the Hevesy method has been estimated in cardiac patients both in the stage of decompensation and after compensation has been restored In decompensated cardiac patients there is an increase not only in the total quantity of blood and plasma but also in the mass of erythrocytes After compensation is restored, both the plasma and blood corpuscles decrease in quantity. There is a difference in the quantity of blood corpuscles, measured in grams per kilogram of dry body weight (the weight of the body when there is no edema), in decompensated patients and in normal subjects In decompensated patients the quantity of erythrocytes, as measured by Nylin and Hedlund, is on the average, 36 4 gm per kilogram of dry body weight, in normal subjects this value is 31.2 gm About the same quantity of erythrocytes is found in compensated cardiac patients as in normal subjects Estimation of the circulation time by this method in cardiac patients with dilated hearts but no peripheral edema supports the view that blood is retained in dilated hearts and that this factor greatly influences the estimation of the circulation time

Nervous Symptoms The symptoms of headache, vertigo, faintness, increased sensitivity to cold, tinnitus or roaring in the ears, black spots before the eyes, muscular weakness and easy fatigability, irritability, lack of power of concentration, and restlessness or drowsiness are essentially of nervous origin It is well to emphasize, however, that chronic irritability of disposition and mental ill health are not necessarily due to anemia.

Paresthesias may be encountered in chronic hypochromic anemia Paresthesias and extensive peripheral nerve and spinal cord disease are common in pernicious anemia

Gastrointestinal Symptoms The symptoms such as anorexia, nausea, flatulence, constipation, diarrhea, and vomiting are symptoms of failing health or accompanying digestive disease but are not necessarily due to anemia Other than the participation of the gastrointestinal tract in the debilities caused by an anemia, there are no symptoms

Genitourinary Symptoms A chronic hypochromic anemia may be caused by menorrhagia Once such an anemia is present, it may remain until the cessation of menstruation Albuminuria is common and there may be evidence of distinct impairment of renal function in those who have anemia There are two reasons for this: (1) A mild chronic glomerulonephritis, a pyelonephritis, or long-standing urinary infection may cause an anemia (2) The anemia itself may impair renal functional activity, for improvement in the anemia may be followed by clearing of the urine An acute glomerulonephritis attended by severe anemia has a poor prognosis Hyperazotemia causes an anemia

Metabolism In severe anemia the basal metabolic rate may be increased In leukemia such an increase is common and may be expected if a low-grade fever is [illegible] fever. A fever

may be increases in the concentration of blood urea (45 to 50 mg per 100 ml. of blood)

CONGENITAL AND FAMILIAL HEMOLYTIC DISEASES

Erythroblastosis. Hemolytic disease of the newborn may be manifested as hydrops fetalis, icterus gravis neonatorum, or congenital anemia of the newborn The condition is caused by iso-immunization of the mother during pregnancy; usually, however, by iso-immunization by an Rh-positive fetus during a previous pregnancy, or by blood transfusion prior to the beginning of pregnancy

The Rh Factor. The ill effects of transfusion of an Rh-negative woman with Rh-positive blood are known only well enough to result in confusion fraught with possible serious consequences Some young couples have been advised not to have children because the husband is Rh positive and the wife Rh negative.

The evidence indicates that an Rh-negative woman married to an Rh-positive man is almost certain to have at least one normal child unless she has received transfusions of Rh-positive blood Transfusions of Rh-positive blood may cause the first child to have erythroblastosis.

Now by appropriate laboratory procedures it is possible to detect Rh sensitization in almost all of the women who have babies with erythroblastosis Detection of sensitization during pregnancy often means erythroblastosis in one of its forms in the infant The exception to this rule occurs in women in whom antibodies have been formed during a previous pregnancy It is well to know about the presence of such antibodies in a multipara, for a sudden increase in antibodies indicates the presence of an Rh-positive fetus with likelihood of erythroblastosis. In such instances, it is only a likelihood, for there are women in whom antibodies were demonstrated during pregnancy who gave birth to healthy Rh-positive infants.

PATHOLOGY Icterus, edema, pallor, effusions in the serous cavities and sometimes petechiae are present Extramedullary hematopoiesis is present in the liver, spleen, kidneys, and adrenal glands In the macerated fetus the finding of erythroblasts in the pulmonary capillaries may be diagnostic The liver and the spleen are enlarged and there is hyperplasia of the bone marrow

SYMPTOMS Unless the mother has been immunized from blood transfusion of Rh-positive blood, the first one to three children may be unaffected However, once the disorder has appeared, succeeding pregnancies terminate in the birth of either an affected infant or a macerated fetus

An anemia present at birth, in the absence of hydrops or icterus, may be referred to as congenital anemia of the newborn In this form of the disease, if the child lives, there are dyspnea, cardiac enlargement and systolic cardiac murmurs if the anemia is severe

In the hydropic form, in which there is a generalized edema of the fetus, the disease is usually fatal prior to birth There is effusion in the pleural, pericardial and peritoneal cavities The liver is enlarged

In the icteric form of the disease the child is born alive and jaundiced at birth, or the icterus appears within one or two days. The spleen and the liver are enlarged

In some instances features of each of the three forms of the disease may be present

Less frequent manifestations of the disease are purpura and melena. When there is melena, there is hepatic and splenic enlargement, and perhaps hepatic cirrhosis

Cerebral symptoms may be present and due to spontaneous intracerebral hemorrhages The cerebral signs consist of convulsions, twitchings, opisthotonos and respiratory difficulties If the infant survives, there may be choreo-athetosis, extrapyramidal spasticity and mental retardation

The development of *kernicterus* has been attributed to the formation of small clumps by the agglutinated erythrocytes which plug the smaller arterioles of the brain to produce ischemic infarcts and to damage the liver It has been suggested that in the presence of jaundice the anoxemic ganglion cells of the nuclear masses take up the bilirubin, thus becoming stained in vivo

Congenital anemia of the newborn infant is often present at birth and it is not accompanied by hydrops or jaundice Often the infant lives only a few days However, if it survives, the anemia is well developed by the third or fourth day and is more marked by the end of a week. If there continues to be a severe anemia, the heart enlarges.

Icterus neonatorum, in contrast to icterus gravis, usually has its onset about the third day after birth and is not associated with severe anemia or enlargement of the liver and spleen. The number of nucleated cells in the circulating blood is not greater than the leukocytes and even these disappear within two or three days.

EXAMINATION The findings on physical examination depend on the manifestations which have been enumerated There may be a green coloring of the deciduous teeth due to deposition of pigment in the enamel. Roentgenographic examination reveals markedly increased density of the bones.

The nucleated erythrocytes of every stage of maturation are present in large numbers They greatly exceed the leukocytes in number even though there is a leukocyte count of from 15,000 to 30,000 per cubic millimeter. The erythrocytes are macrocytic and well filled with hemoglobin The hemoglobin concentration is normal Often by the third or fourth day of life the erythrocytes have decreased in number, and a profound anemia may be present.

The van den Bergh reaction may be indirect if damage to the hepatic cells and obstruction of the bile ducts have not occurred

DIAGNOSIS. A definite diagnosis can be made only if there is an appropriate combination of agglutinogens and agglutinins in the mother, the child and the father If a woman has erythrocytes which are Rh-negative and if she has had a stillbirth or miscarriage after one or two normal deliveries, or if she has had blood transfusions and since these transfusions has had an abortion, *erythroblastosis fetalis* is suspected Roentgenologic examination may be diagnostically helpful if there is revealed a "halo" about the fetal head due to edema of the scalp.

The most important factor from the standpoint of the life of the child is the readiness of suitable Rh-negative blood for transfusion.

Erythroblastic Anemia (Cooley's Anemia, Thalassemia). Erythroblastic anemia begins in early life, and in the United States persons affected are of Italian, Greek, Syrian or Armenian parentage

The etiology of aberrations of the erythrocytes in erythroblastic anemia is not established. The anemia represents a hereditary anomaly of the erythrocytes which is inherited as a recessive characteristic In the heterozygous individual the symptoms are mild, if present at all (thalassemia minor) The disease arises when both parents are affected and the homozygote, the patient, manifests the anemia (thalassemia major). It has occurred in identical twins

PATHOLOGY. There are present an increased destruction of erythrocytes, a bone marrow hyperplasia, a liberation of immature erythrocytes, a hemolytic process of a compensatory nature, and a defect in pigment metabolism. There are evidences of an active formation of blood, both medullary and extramedullary, splenomegaly, changes in the bones, and pigmentation of various organs resembling that of hemochromatosis The erythrocytes seem to be formed with an adequate or excessive membrane so that they can absorb more fluid without bursting than can normal cells.

SYMPTOMS. The child has been pale and weak since birth In many instances there has been a gradual enlargement of the abdomen with loss of weight. Often the disease is found when the child is examined on account of the symptoms of acute infection or disease.

EXAMINATION. The child has a large head and is small for its age The cheek bones and the cranial bones are thickened, the bridge of the nose is small, the eyelids are puffy, and there may be an epicanthal fold (mongoloid facies). The skin is pale and yellowish brown Cardiac dilatation is often present, and in advanced stages there are edema and effusion into serous cavities and ecchymoses. Spontaneous bleeding may be present. The abdomen may be large and often there is ascites The liver and especially the spleen are enlarged There is often edema of the legs and feet

Roentgenograms reveal changes in the skull, the frontal bones, the metacarpals, and the distal ends of the femora The changes consist of medullary trabeculations and thickening of the skull with thinning of the outer and inner tables, osteoporosis, and perpendicular striations of the diploe

The anemia is a hypochromic, microcytic type, and nucleated erythrocytes are present and may be numerous The majority of the nucleated erythrocytes are normoblasts and microblasts The van den Bergh reaction is positive, indirect

The leukocytes are increased in number, counts of 10,000 to 25,000 per cubic millimeter being common There may be present myelocytes and myeloblasts

DIAGNOSIS The important features of the disease diagnostically are mongoloid facies, splenomegaly, skeletal changes and severe anemia The erythrocytes are thin and of various shapes and sizes. Erythroblastosis, polychromatophilia, stippling, reticulocytosis, leukocytosis and slight icterus are usually present.

The resistance to hemolysis by hypotonic saline solution distinguishes the condition from congenital hemolytic jaundice and from sickle cell anemia The racial and familial incidence helps to distinguish Cooley's anemia from other erythroblastic anemias which may be present in infants and very young children

The fully developed disease is fatal An intercurrent infection is the usual cause of death In less severe instances death does not occur The degree of severity ranges from the comparatively fulminating disease seen in infancy to a benign anomaly producing little or no impairment of health which may be present at any age (the so-called thalassemia minor)

Thalassemia Minor. Thalassemia minor is observed in adolescents and adults of Mediterranean ancestry It has the features of thalassemia major, but they are of a much milder degree It too is apparently an inherited defect in hemoglobin synthesis resulting in cells of poor grade which nevertheless possess more than adequate membrane, so that they can absorb more fluid than normal cells without bursting Because of their thinness, they appear as bizarre forms

These patients usually have hypochromia and microcytosis of the erythrocytes with or without anemia and occasionally associated with abnormally high erythrocyte counts Stippled, oval cells, out of proportion to the degree of anemia, are the morphologic abnormalities present in the red corpuscles The resistance of the erythrocytes to hemolysis in hypotonic sodium chloride solutions is increased. The anemia is refractory to iron therapy Splenomegaly and slight icterus may be present

Sickle Cell Anemia. Sickle cell anemia is a hereditary and familial form of chronic, hemolytic anemia In addition to the anemia there are rheumatoid manifestations, leg ulcers and acute paroxysms of pain The characteristic shape that the erythrocytes assume in sickling is an abnormality of the cells and not of the blood plasma

Sickle cell anemia is apparently the only known disease that is completely confined to a single race, the Negro race Many instances of sickle cell anemia had been demonstrated in American Negroes before the disease was found to occur in Africa, the accepted place of its origin

The true sickle cell anemia or its related condition, sicklemia, occurs only in Negroes, Cubans, Mexicans, Italians, Greeks, Arabs, Portuguese, Egyptians and

South Americans The people other than Negroes in whom the disease is found are either members of the so-called Mediterranean races who, anthropologists say, as a result of their proximity to Africa have acquired a considerable admixture with the Negro race, or are white Americans whose families have at some time lived in or near the former slave states or metropolitan areas. The slave trade with Africa, participation of Negroes in European wars, and other circumstances of history brought the Negro race into close contact with many groups of white people and resulted in a wide diffusion of African stock. Ogden has expressed his conviction that the presence of the trait is a definite proof of an admixture in the immediate or remote ancestry

Several theories of the genetics of sickle cell anemia have been advanced. The homozygous-heterozygous theory suggests that there is a gene in Negro populations which when heterozygous results in sicklemia and when homozygous results in sickle cell anemia, a situation analogous to that which exists in familial erythroblastic (Cooley's) anemia

Sickle cell anemia has been diagnosed in infants less than 1 year of age but usually occurs in young adults There is no sex predisposition.

PATHOLOGY The spleen loses its normal structure and becomes infarcted, fibrotic and atrophic. The changes increase until the organ becomes a small fibrotic mass. The liver is enlarged and congested The bone marrow is hyperplastic The cortex of the bone is thickened and sclerotic but shows areas of medullary invasion and of necrosis Hemosiderosis is found in the kidneys, liver, spleen, lymph nodes and bone marrow.

SYMPTOMS Weakness and fatigability are commonly present. Episodes of pain in the joints or in the extremities often occur. Severe, stabbing, abdominal pain of sudden onset may be referred to any part of the abdomen Prostration and abdominal distention may be associated, and these symptoms may simulate those of an abdominal emergency. The leukocytosis which is usually found in patients who have this disease only adds to the diagnostic difficulty when an acute abdominal condition is suspected which seemingly should be treated surgically

Attacks of pains in the extremities are common but are rarely associated with redness, tenderness or swelling of the joints.

Sickle cell anemia progresses to an ultimately fatal outcome Death may occur from infections, cardiac or renal failure, and thrombosis or hemorrhages involving vital tissues Gallstones may form and cause symptoms

EXAMINATION. In sickle cell anemia the patients are usually underweight, the trunk is short, the extremities are long, and the habitus is linear with comparatively narrow hips, shoulders, hands and feet Kyphosis, scoliosis, saber shins, and tower-shaped skulls may be observed In both children and adults there may be an increased upper thoracic kyphosis and lumbar lordosis and the thorax may be increased in anteroposterior diameter The scleras are jaundiced There may be fever and generalized abdominal tenderness, and palpable liver and spleen Chronic unilateral or bilateral leg ulcers over the malleoli may be present These ulcers are deep and usually single, but multiple ulcers sometimes are present

The heart is enlarged, and a systolic murmur of variable intensity, depending on the degree of anemia, is often present

If the patient is critically ill, neurologic findings such as paresthesias of the extremities, drowsiness, stupor or coma, hemiplegia, aphasia, convulsions, stiffness of the neck, irritability, nystagmus, pupillary changes, blindness (temporary or permanent) and cranial nerve palsies may be present. The cerebrospinal fluid is usually normal

Examination of the blood may reveal a severe anemia The anemia is usually normocytic but in some instances, in severe anemia, it may be macrocytic. A reticulocytosis, nucleated erythrocytes, polychromatophilia, basophilic stippling, and sometimes Howell-Jolly bodies are present.

The characteristic phenomenon in this disorder is the change which can be observed to take place in the shape of the erythrocytes *when a drop of blood is sealed under a coverslip on a slide or in test tubes* In such preparations a few bizarre, multipointed forms (sickling) may be seen immediately, but changes occur at a maximal rate in 2 to 6 hours after the blood is drawn.

Leukocytosis is regularly present in sickle cell anemia It may be marked when excessive blood destruction is going on There is often a shift to the left, and there is a moderate number of myelocytes. Eosinophilia is not infrequent and the monocytes may be increased in number

Platelets are increased in number (300,000 to 500,000 per cubic millimeter) and bizarre forms may be observed The *sedimentation* of the corpuscles is slow. There are *hyperbilirubinemia* and increased urobilinuria of varying degree. The van den Bergh reaction is indirect Studies of bone marrow do not distinguish this from other forms of hemolytic anemia

DIAGNOSIS Diagnosis of sickle cell anemia is made by observing sickling of the erythrocytes in wet preparations, in conjunction with an anemia and signs of active erythrocytic regeneration, leukocytosis, and bilirubinemia Sickling alone is not sufficient, for it only indicates the presence of the sickle cell trait which may be the only abnormality present In a Negro patient who has severe abdominal pain, muscle spasm, leukocytosis and anemia the blood should be tested immediately for sickling before the appendix is removed or the pelvis is surgically explored.

Familial hemolytic jaundice has much in common with sickle cell anemia but, in addition to being very rare in Negroes, it is characterized by increased fragility rather than increased resistance of the erythrocytes in hypotonic saline solutions.

Congenital Hemolytic Jaundice. This chronic form of hemolytic anemia and jaundice is known also as chronic familial jaundice (icterus) hemolytic splenomegaly, chronic acholuric jaundice, and spherocytic or globe cell anemia

The disease is characterized by splenomegaly, spherocytosis, and diminished resistance of the erythrocytes to hemolysis by hypotonic saline solutions The disorder may not be sufficiently severe for recognition until late adult life

ETIOLOGY Genealogies of three and even four generations reveal that the trait is a mendelian dominant and is transmitted by either parent Some of the offspring are free of the disease.

PATHOLOGY It seems that the fundamental abnormality is an unusual thickness of the erythrocytic walls so that the cell approaches a sphere in shape, these spherical cells are easily destroyed by the spleen Surgical removal of the spleen thus removes the source of erythrocytic destruction

The *spleen* is enlarged, free of adhesions and weighs 1,000 to 2,000 gm The *liver* usually is not enlarged, nor is it usually cirrhotic, but the quantity of iron pigment may be increased Gallstones may be present in the gallbladder. The *kidneys* and the *lymph nodes* may contain increased blood pigment (hemosiderosis)

The *bone marrow* is hyperplastic *Heterotopic masses of bone* have been observed alongside the vertebral column in the thorax and in the renal pelvis

SYMPTOMS The symptoms may be manifested at birth or in childhood or adolescence

The icterus is not intense The complexion is constantly sallow. Increase in destruction of blood may be of sudden onset and is manifested by fever, palpitation and shortness of breath Extensive episodes of blood destruction are accompanied by violent abdominal pain and vomiting Once severe jaundice and anemia have developed, complete spontaneous remission is unusual. The jaundice is not accompanied by itching of the skin.

The symptoms of *cholelithiasis* are common Cholelithiasis is present in one half or more of these patients

EXAMINATION The *spleen* is enlarged During latent periods of the disease the spleen may be difficult to palpate. The enlarged spleen may attract attention by

producing a sense of oppression or weight, due to its size, or it may be the site of a sudden attack of pain. The *liver* is often slightly enlarged.

Chronic leg ulcer may be present over the internal or external malleoli.

The *tower skull* (*Turmschädel*) *is perhaps the commonest skeletal* anomaly. Other developmental anomalies may be present The changes in the bones demonstrable by roentgenologic examination are similar to those observed in sickle cell anemia and erythroblastic anemia

The fragility of the red corpuscles in hypotonic saline solutions is increased The anemia is of moderate degree or is absent A rapid fall to as few as 1,000,000 erythrocytes per cubic millimeter of blood may occur during one hemolytic crisis Reticulocytes are increased in number Polychromatophilia, normoblasts and microblasts are present The leukocyte count is normal, except during a hemolytic crisis when there is leukocytosis and a shift to the left

In the presence of deep jaundice the hemoglobin cannot be accurately determined The van den Bergh reaction is indirect, sometimes biphasic.

The urine contains increased amounts of urobilinogen, urobilin and coproporphyrin The stools contain bile pigment as well as excessive quantities of urobilin. The bone marrow obtained by sternal puncture reveals erythropoietic hyperplasia of the normoblastic type

False positive serologic reactions for syphilis may be revealed in congenital hemolytic jaundice They usually disappear following splenectomy.

DIAGNOSIS The combination of increased fragility of erythrocytes, hemolytic *anemia, reticulocytosis, spherocytosis, splenomegaly and jaundice and often* gallstones is diagnostic Gallbladder disease with gallstone in relatively young persons is suggestive of congenital hemolytic jaundice in whites and sickle cell anemia in Negroes.

Death may occur during a hemolytic crisis. Many patients, however, attain an advanced age despite the chronic anemia. A prolonged spontaneous improvement without jaundice may last until late adult life Once jaundice has supervened, it does not clear up until the spleen has been removed

Hemolytic Jaundice in Adults. There is *little* justification *for considering the* acquired form of hemolytic jaundice as a distinct clinical entity These patients are probably manifesting the same disease as that designated as congenital hemolytic jaundice, for in these patients there is a latent inherent defect in the erythrocytes permitting easy hemolysis, which awaits some infectious, toxic or *metabolic disturbance* to make the defect apparent

The acquired hemolytic jaundice comprises those forms which seem to be identical with the congenital form of the disease, with the exceptions of those which are secondary to some such disease as syphilis, tuberculosis, septicemia, leukemia, Hodgkin's disease, and cirrhosis of the liver If recovery from the primary disease should occur, the hemolytic jaundice disappears

The symptoms may be the same as those of the congenital form, namely, a progressive anemia, or a sudden onset with fever, prostration, abdominal pain, jaundice and anemia The hemolytic crises are more frequent and more severe. The anemia and pallor are more pronounced than the jaundice

The *symptoms* vary from those of a rapidly developing and fatal disease to those of a chronic disorder. In some instances in which the clinical symptoms resemble those of the congenital disorder, not only is the family history negative but examination of the blood of various members of the family reveals no evidence of a familial disorder

On examination the skin is pale and slightly jaundiced The spleen is enlarged There is spherocytosis Increased fragility of the erythrocytes is less common than in congenital hemolytic jaundice and may be present in but slight degree or not

at all. There are reticulocytosis and leukocytosis just the same as in the congenital form of the disease.

The diagnosis is based on the preceding blood findings. When the diagnosis is made, splenectomy should be performed

ACQUIRED HEMOLYTIC ANEMIA

The hemolytic diseases of congenital or hereditary origin were described in the pages immediately preceding this discussion In these diseases there is some inherent defect in the constitution, or in the maintenance of the erythrocytes.

In all forms of hemolytic anemia the changes present in the blood and bone marrow in either the acute or chronic forms represent the products of destruction of blood and its effects on the stimulation of the marrow and the tissues responsible for the removal of the residua of hemolysis Splenomegaly and demonstrable abnormalities in bone structure, the effects of long-continued overactivity of the spleen and bone marrow, are regularly present

In the more acute stages of hemolytic anemia there is an excessive destruction of erythrocytes, and anemia of varying degrees ensues Jaundice is a regular manifestation when there has been a sufficient hemolysis to liberate adequate amounts of pigment, and likewise, if there is excessive destruction, hemoglobinuria is present. If the bone marrow is normal, there is evidence of erythrocytic regeneration and leukocytosis.

There are many different kinds of hemolytic agents to cause acute and chronic hemolytic anemias These agents are the same as those listed as the cause of jaundice (see Jaundice, Chapter 13)

A common cause of acute hemolytic anemia in tropical and subtropical climates is malaria. The anemia is due to the destruction of red corpuscles by the plasmodium and to the toxic inhibition of the bone marrow activity The severity of the anemia may be partially correlated with the intensity and duration of the infection

Blackwater fever (black urine, hemoglobinuric fever, hemorrhagic malarial fever, black jaundice, canebrake yellow fever) is the result of chronic malarial infection for which the patient has been inadequately treated with quinine (see p 1291)

Bartonella bacilliformis causes a severe, acute hemolytic anemia.

The *bacterial toxins* from organisms *Clostridium perfringens, Streptococcus hemolyticus* and *Streptococcus viridans* may cause a profound hemolytic anemia which develops so rapidly that in a few days the erythrocyte count is less than 1,000,000 cells per cubic millimeter

The mechanism of the actions of *chemical agents* in the production of the anemia is obscure (see Chapter 19)

Acetanilid or *phenacetin* poisoning, usually obtained from headache medicine, is characterized by cyanosis, anemia, and loss of weight The cyanosis may be due to the formation of methemoglobin or other pigments (paramidophenol derivatives).

When there is an *idiosyncrasy to sulfanilamide*, anemia may appear between 24 and 72 hours after the first administration of the drug The anemia is likely to recur if the drug is administered again The destruction of blood is rapid and is accompanied by fever, jaundice, marked leukocytosis, reticulocytosis and normoblasts

Vegetable poisons are agents in production of hemolytic anemia Inhalation from bean plants (*Vicia faba*) when in blossom or ingestion of fava beans when fresh, causes in sensitive persons an acute hemolytic anemia, favism. The castor bean contains the hemolytic agent, ricin (see p 20)

Among *animal poisons* venom from the pit vipers (rattlesnakes, moccasins and copperheads) of the United States contains a lecithinase which converts lecithin to *lysolecithin*, a powerful hemolytic agent (see p. 1446)

Endogenous hemolysins are formed from the actual heating of the blood following severe burns and sunstroke Hemolysis of the blood is often severe in fatal sunstroke (see p 1477)

Hemolysins of the immune-body type may produce hemolytic anemia and hemoglobinuria. The anti-Rh agglutinins are formed after repeated blood transfusions. In

rare instances the anti-M and anti-P agglutinins also are the cause of *intragroup hemolytic reactions to transfusion.* The iso-immunization of the Rh-negative woman by her Rh-positive fetus, rendering her susceptible to transfusion reactions and producing in the fetus a fulminating and often fatal hemolytic anemia (*erythroblastosis fetalis*), is a recent subject of much conversation (see Transfusion Reactions, p. 795)

There are the cold hemagglutinins In paroxysmal hemoglobinuria e frigore a hemolysin activated by cold is present In nocturnal hemoglobinuria hemolysis depends on an immunologic system. In certain cases of acute hemolytic anemia heat labile autohemolysins requiring complement have been demonstrated.

SYMPTOMS A rapid destruction of blood is manifested by severe pain in the back, abdomen or legs, headache, and chill Synchronous with the chill is fever which rapidly subsides If destruction of blood is excessive, profound prostration and shock ensue. Abdominal pain and melena are common. This is the syndrome of acute hemolysis or hemolytic crisis.

Anuria or oliguria may develop The urine is dark as the jaundice develops. Anemia, weakness and palpitation occur in rapid succession. Reactions to transfusion are common

EXAMINATION The findings in the syndrome of acute hemolytic crisis are well illustrated by paroxysmal hemoglobinuria and hemoglobinemia. Vascular disturbances characterized by vasoconstriction are present. Thrombosis and gangrene may be observed Infarcts in the spleen and the lungs are manifested by enlarged spleens, consolidated areas in the lungs and hemiplegias Thrombosis of the arteries and veins of the extremities may be observed

A rapid destruction of blood liberates hemoglobin in the blood plasma. The van den Bergh reaction is indirect and the concentration of serum bilirubin is increased. The intensity of bilirubinemia depends on the extent of destruction of blood and on the capacity of the liver to remove the pigment from the blood stream and excrete it in the bile If hemolysis is severe, hemoglobinemia ensues Hemoglobin, when once present in the urine, persists until the plasma concentration is decreased to 30 to 50 mg. per 100 ml

Pigments other than hemoglobin may appear in the blood plasma Hemoglobinemia and methemalbuminemia invariably are associated with bilirubinemia When the destruction of blood is less rapid, only bilirubinemia is present

The urine contains albumin and granular and red cell casts

There are signs of active erythrocytic regeneration Reticulocytes are increased in number There are polychromatophilia and numerous normoblasts and macroblasts

Microcytes, which show no central pallor when stained, are characteristic of familial hemolytic jaundice.

In this disease the *fragility of the erythrocytes,* when suspended in hypotonic solutions of sodium chloride, is greatly increased Increased fragility in hypotonic saline solutions is unusual in other forms of hemolytic anemia.

There are leukocytosis and a shift to the left, and myelocytes and even myeloblasts may be present Platelets are numerous and large. The bone marrow is hyperplastic.

DIAGNOSIS The diagnosis depends on the history and findings as enumerated

Chronic Hemolytic Anemia. Chronic hemolytic anemia is manifested by jaundice (see Chapter 13).

NORMOCYTIC ANEMIA

In normocytic anemia the erythrocyte maintains its normal size, shape and color.

The causes of normocytic anemias may be divided into two large categories: (1) sudden loss of blood from hemorrhage and (2) decreased blood formation

The causes of *sudden losses of blood* are numerous and often obvious, but in some instances the cause is indeterminable.

The *rapid loss of 2 liters of blood* may cause immediate death, whereas this amount, or even more, of blood lost over a 24-hour period may be tolerated

The immediate cause for *decreased formation* is failure of bone marrow to produce, as when it becomes replaced with fat or becomes inactive from any cause The commonest cause of marrow inactivity is the toxic effects from infection and exhaustion during the course of chronic disease In some instances blood formation is hindered by infiltration of marrow with neoplastic growths There are both relative and absolute normocytic anemias A relative normocytic anemia is produced by an increase in the amount of plasma, an hydremia, without alteration in the total quantity of erythrocytes In contrast with the hydremic state is the concentration of normocytes in dehydration.

SYMPTOMS. When the loss of blood has been moderate (500 ml), unless the patient rises or attempts to walk there are no symptoms On the patient's arising, the pulse rate accelerates and the blood pressure tends to fall The feeling of weakness and dyspnea occur only on physical exertion

When more than 500 ml of blood is lost, on sitting up faintness and syncope, accompanied by bradycardia, may ensue A loss of large amounts of blood causes shock (see p. 792)

The severity of the hemorrhage cannot be determined during the first symptoms of loss of blood because vasoconstriction accompanied by a continuing dilution of the blood by body fluids passing into the vessels produces constantly changing values. In rare instances hemorrhage into the intestinal tract is followed by digestion of blood, and the concentration of urea nitrogen in the blood may increase However, in practice this is rare Hemorrhage into one of the body cavities or into a cyst followed by reabsorption of the products of hemoglobin may produce jaundice. Moderate fever may accompany gastrointestinal hemorrhage High fever occurs when there is escape of blood into muscles, parenchymatous organs or body cavities.

EXAMINATION Within the first hour after a hemorrhage there are an increase in the platelet count and a shortening of the coagulation time. Within 5 or 6 hours polymorphonuclear leukocytosis is present (10,000 to 20,000 per cubic millimeter) There is a shift to the left in the myeloid series, and myelocytes make their appearance. Reticulocytes begin to increase within 24 to 48 hours The maximal number (5 to 15 per cent or higher) is reached within a week

The erythrocyte count and the value for hemoglobin are high and then decrease. Normoblasts and polychromatophilia appear after several days if the hemorrhage has been severe The value for the hemoglobin content is the most valuable and the most practical to obtain Continued bleeding is suggested by high count of reticulocytes and leukocytes continuing after the first week subsequent to the hemorrhage

In the healthy person blood regeneration is rapid and the hemoglobin reaches normal limits after 6 to 8 weeks, even after severe hemorrhages.

DIAGNOSIS An anemia is diagnosed when the values for the hemoglobin and the total erythrocyte count are less than normal A severe anemia, when the cause is not obvious, before the age of 50 years, usually originates in the alimentary tract in men and in the genital organs in women

Anemias of Decreased Blood Formation. There may be a decreased blood formation in cachexias, infections with or without fever, nutritional deficiency, aplastic anemia from any cause, and an invasion of the bone marrow by malignant tissues, producing the so-called myelophthisic anemias Finally, there are anemias arising from decrease or lack of blood formation when the marrow is hyperplastic The reason for this origin of anemia is unknown.

Aplastic Anemias. These anemias are designated progressive hypocythemia, aregeneratory anemia, aleukia haemorrhagica, panmyelophthisis, hypoplastic anemia, and toxic paralytic anemia

Aplastic anemias are of two types, primary and secondary.

Primary Aplastic or Refractory Anemia. This is a severe anemia accompanied by granulocytopenia and thrombocytopenia which will not respond to any treatment except the transfusion of whole blood. Anemia of this type is not the result of infection, chronic renal or hepatic disease, malignant disease, malnutrition, or physical or chemical agent It results from either inborn or acquired endogenous factors. In the young patient there may be present increased pigmentation of the skin, hypoplasias of the gonads, and other developmental anomalies. The disease in the young person has been termed *idiopathic aplastic anemia.*

There is bleeding from the mucous membrane, pharynx and gums. The hemorrhage depends in part on the degree of granulocytopenia and thrombocytopenia If the progress is slow, there may be only progressive weakness and fatigability. If the disease progresses rapidly, there are high fever and anoxemia When the anemia becomes well established, there are bleeding from the nose, mouth, or gastrointestinal tract, menorrhagia and purpura.

There may be purpuric spots in the skin There is pallor of the skin and mucous membranes. Retinal hemorrhages are often present The spleen is not palpable In those in whom the bone marrow is hyperplastic the circulating blood reveals no signs of regeneration. The erythrocyte count is often as low as 2,000,000 and the leukocyte count 1,500 per cubic millimeter There are leukopenia and thrombocytopenia. An absolute lymphocytopenia is present, for the monocytic and granulocytic series of cells are gone The coagulation time is normal The bleeding time is prolonged and the blood clot retracts poorly

The diagnosis is based on the presence of anemia, leukopenia and thrombocytopenia In differential diagnosis it is necessary to consider aleukemic leukemia. Idiopathic aplastic anemia in time proves fatal despite blood transfusions

Secondary Aplastic Anemia Due to a Chemical or a Physical Agent. A secondary aplastic or refractory anemia may follow the administration of or the exposure to certain chemical or physical agents (see Chapter 19)

Simple Chronic Anemia (Secondary Anemia). A simple chronic anemia is associated with the majority of infections It is often insidious in its inception and frequently responds slowly to treatment. It is often a normocytic anemia.

The name chronic secondary anemia has been and still is employed for this type of anemia Hematologists object to the use of this term because of the fact that any anemia from any cause is secondary

A simple chronic or secondary anemia occurs in most instances of subacute and chronic inflammatory disease For instance, osteomyelitis, chronic ulcerative colitis, ileitis, pelvic inflammatory disease, infections of the urinary tract, bronchiectasis and pulmonary abscess often are associated with a simple chronic anemia About two thirds of those who have a subacute *Streptococcus viridans* endocarditis have an anemia which may be severe

Anemia is almost always coexistent with nitrogen retention It may be present in an acute or a chronic nephritis when there is no increase in the concentration of urea nitrogen in the blood Anemia is not related to the type of renal disease. It may occur in acute or chronic nephritis, in congenital cystic renal disease, or in urinary retention In an acute urinary retention, without an increase in the concentration of blood urea in the beginning, for instance, from an enlarged prostate, if there is an anemia, it is suggestive of some disease other than benign prostatic enlargement

Infestation by *parasites*, with the exception of hookworm infestation, usually does not cause anemia Anemia in hookworm infestation, when present, probably is the result of chronic loss of blood When anemia is encountered in amebiasis, the cause is nutritional disturbance, loss of blood, or secondary infection In infestation with *Schistosoma mansoni* there may be hypochromic microcytic anemia in the intestinal phase or macrocytic anemia when cirrhosis of the liver develops. Anemia in malaria is hemolytic in origin and is considered with the hemolytic anemias

Aberrations in *intestinal absorption* are rarely responsible for the development of anemia in intestinal disorders accompanied by diarrhea If anemia develops in these disorders, its origin is from intestinal bleeding which almost always is present. For instance, a patient may have a functional disorder characterized by a diarrhea for years and not become anemic.

Nutritional deficiency may produce macrocytic anemia, hypochromic microcytic anemia and perhaps normocytic anemia The importance of the lack of any particular vitamin in the production of anemia is not known except for vitamin B_{12} deficiency (see Pernicious Anemia, p 844)

Anemia of the so-called physiologic variety is common in *pregnancy* This type of anemia may be present by the eighth week and may progress until about the twenty-second week and then become stationary Even in this anemia a reduction in hemoglobin to less than 10 gm per 100 ml of blood is worthy of concern. In the puerperium the erythrocyte count and volume of packed red cells increase rapidly, but the hemoglobin returns to within normal limits more slowly

Malignant disease does not directly cause anemia through the action of toxins or hypothetic substances. Malignant disease in the alimentary tract often causes anemia through loss of appetite as the result of interference with digestion and absorption, or because of loss of blood If chronic loss of blood is sufficient, hypochromic microcytic anemia ensues When metastasis occurs, and the bone marrow is involved, myelophthisic anemia is characteristically present

Simple chronic or secondary anemias of mild degree are usually symptomless. Any symptoms present are those of the primary disease. In severe grades of anemia the symptoms are in accord with the rapidity of development A patient may have a severe anemia with few or no symptoms if the anemia has developed slowly over a period of months or years

There may be pallor from confinement or from anemia. Skin pallor alone or combined with pallor of mucous membranes is not a good criterion for the presence of anemia

The reduction in the number of erythrocytes, the quantity of hemoglobin, and the volume of packed red cells corresponding in degree are the indications of anemia

The diagnosis of a simple chronic (secondary) anemia is based on a reduction below normal of the erythrocytes (5,000,000 for men and 4,500,000 for women) and the hemoglobin (below 14 gm. per 100 ml of blood for men, and 12 gm for women) In the normocytic anemias the volume of the packed cells is decreased in direct proportion to their [illegible]

Myelophthisic Anem [illegible]

of anemia associated with [illegible] of the conditions thus designated are erythroleukemia, aleukemic leukemia, leukemia with osteosclerosis, leukoerythroblastosis, megakaryocytic myelosis, osteosclerotic anemia, aleukemic megakaryocytic myelosis, myeloid megakaryocytic hepatosplenomegaly, chronic nonleukemic myelosis and agnogenic myeloid metaplasia

Metastatic carcinoma in bone marrow is perhaps the commonest cause of this type of anemia *Multiple myeloma* causes an occasional case In very rare instances a myelophthisic anemia is caused by *myelosclerosis* (osteosclerosis myelofibrosis) or by osteopathia condensans disseminata, in which there is an irregular increase of fibrous or bony tissue in the bone marrow Myelophthisic anemia may occur in a hereditary disorder known as *marble bones* (ivory [illegible]

A myelophthisic anemia is encoun[illegible] *xanthomatoses,* Gaucher's disease, [illegible] osteitis deformans, osteitis fibrosa cystica, osteomalacia, osteogenesis imperfecta cystica, in *poisoning* by fluorine or phosphorus, and after prolonged administrations of anterior pituitary extract, parathyroid extract, estrogens and irradiated ergosterol and in hyperparathyroidism

Deep bone pains, abdominal pain, epistaxis, loss of weight and weakness are

common symptoms. There may be palpitation, dyspnea or purpura. The symptoms may be such as to suggest the underlying disease.

Splenomegaly may be the only finding on examination except the anemia There may be tenderness along the long bones, Bence Jones protein in the urine, and rouleaux formation of the red cells in the smears. The total amount of serum protein is increased An anemia exists in variable degree characterized by the presence of normoblasts in the circulating blood in numbers out of proportion to the severity of anemia Reticulocytes are increased, and polychromatophilia and stippling may be present

The total and differential counts of cells of the myeloid series maintain their normal proportions. Variable numbers of myelocytes and myeloblasts may be present The platelet count may be normal or moderately reduced, or in some a thrombocytopenia may be present.

Myelophthisic anemia is suspected whenever nucleated erythrocytes or myelocytes are observed in the circulating blood in those who have little anemia. A myelophthisic anemia is suspected if the total serum protein exceeds 8 gm. per 100 ml, if Bence Jones protein is found in the urine, or if rouleaux formation of the erythrocytes is observed in the blood smears. The diagnosis depends on positive evidence of distortion of bone architecture by means of roentgenologic examination in association with the foregoing enumerated blood findings

PERNICIOUS ANEMIA AND OTHER MACROCYTIC ANEMIAS

Pernicious Anemia. Pernicious anemia is called also Addison's anemia, Biermer's anemia, Addison-Biermer anemia, and Biermer-Ehrlich anemia

Castle has recently concluded that the information presently available suggests that addisonian pernicious anemia is the clinical result of a deficiency chiefly of vitamin B_{12} This deficiency is predominantly due to a lack of gastric secretion, itself usually a manifestation of hereditary predisposition and of advancing age In some patients local disease or surgical ablation destroys this essential function of the stomach The consequent failure of vitamin B_{12} to be assimilated affects hematopoiesis adversely and frequently also the integrity of the alimentary tract and of the nervous system The proximal cause of the macrocytic anemia is both decreased production and increased destruction of defective red cells Either both processes must be of only moderate degree, or the magnitude of each must be inversely related to that of the other

Defective diets and intestinal dysfunction or disease, especially when gastric secretion is not significantly disturbed, may result in nutritional macrocytic anemia in which the predominant deficiency is not of vitamin B_{12} but of pteroylglutamic acid Dietary deficiency of ascorbic acid probably restricts the formation of the metabolically active and closely related form of pteroylglutamic acid known as the citrovorum factor, or folinic acid. Vitamin B_{12}, pteroylglutamic acid and ascorbic acid are apparently required for normal hematopoiesis

Pernicious anemia affects chiefly, but not exclusively, the white race. Racial and hereditary influences appear to be of chief importance in its incidence and distribution The inherited feature of the disease is manifested by achylia gastrica. Achlorhydria is not the essential factor, but its presence is necessary for the diagnosis Achlorhydria is present in many who do not have pernicious anemia

The disease has been described in single ovum twins. Pernicious anemia has occurred in the men, and chronic hypochromic anemia in the women of some families

Men and women are affected equally The disease is rare in persons less than 20 years old. The greatest incidence is after 40 years of age.

Those who have pernicious anemia may appear to be of the same constitutional

type. They are often short and have a deep short thorax, blue or light-colored eyes, and gray or white, fine-textured hair which has lost color prematurely

Pernicious anemia is often associated with infections and arteriosclerosis, which tend to impair the response to liver therapy It may be associated with diabetes mellitus, which has in common with pernicious anemia atrophy of the mucous membrane of the tongue, diarrhea, and neurologic disturbances Any condition which destroys the absorptive portions of the stomach, such as carcinoma or total or subtotal gastric resection, may cause anemia having many of the characteristics of pernicious anemia Rigler and Kaplan report in a series of necropsies (22,231) at the University of Minnesota on subjects 45 or more years of age that evidence of pernicious anemia was discovered in 293 In 36 of these there was carcinoma of the stomach. This incidence of carcinoma of the stomach was more than three times greater than the normal morbidity rate for carcinoma of the stomach The Minnesota investigators found that 12 per cent of the deceased patients who had pernicious anemia had carcinoma of the stomach, and 7 1 per cent had benign polyps.

Symptoms Often the initial symptoms are general weakness, sore tongue, and numbness or tingling of the extremities Commonly the patient complains of faintness, stiffness of the legs and difficulty in walking, headache, nausea, lack of appetite, vomiting, dizziness, shortness of breath, palpitation, loss of weight, pallor, abdominal pain, diarrhea and sore tongue

Soreness and a burning sensation affect the anterior half of the tongue The glossitis may appear before there is a known anemia, or it may portend a relapse and thus indicate inadequate treatment

Diarrhea occurs but is not common It is doubtful that achlorhydria is ever responsible for such a diarrhea The other complaints referred to the gastrointestinal tract are inconstant They are anorexia, nausea, "gas," a sense of fullness in the epigastrium, heartburn, vomiting, and irregular but usually not intense abdominal pain unless a visceral crisis secondary to the changes in the spinal cord occurs.

In those who have a severe anemia, congestive heart failure may ensue However, degenerative cardiac disease is not often due to pernicious anemia It is usually due to degenerative vascular changes occurring in the age group affected by this anemia. When vascular symptoms, such as those of intermittent claudication, result from pernicious anemia, relief follows adequate treatment and maintenance therapy. Cardiac symptoms occur because, during anemia, the circulation time is shortened as the result of increased heart rate and there is a greater output per beat and consequently the amount of work done by the heart per minute is increased. In the presence of greatly decreased concentration of hemoglobin angina pectoris, alone or accompanied by congestive failure, may develop These cardiac ailments are precipitated by oxygen want, for there is not enough hemoglobin to carry sufficient oxygen to supply the tissues

In the presence of severe anemia fever is present which disappears as the anemia is relieved

Complaints referable to the nervous system are present in 9 of every 10 patients who have pernicious anemia

The symptoms referable to the nervous system may occur while anemia is mild or even absent There may be irritability, lack of concentrating power, dullness, drowsiness, and depression If there are changes in the spinal cord, pyelitis and cystitis are frequent complications due to an inability to empty the bladder.

The special senses may be disturbed by, for instance, tinnitus, visual defects and retinal hemorrhages Optic atrophy is rarely observed and, like the symptoms of combined sclerosis of the spinal cord, it may be the first symptom

EXAMINATION. The loss of body weight is slight. Often the *skin* is smooth and inelastic. When the anemia is severe, the skin is dry, and is yellowish, as are the scleras. There may be diffuse or blotchy brownish pigmentation and large areas of leukoderma over the dry smooth skin.

The epithelium of the tongue is devoid of circumvallate papillae. Atrophy of these papillae is characteristic, and papillae which have atrophied for any reason do not return to normal size under treatment. Smooth, glazed-appearing tongues are most frequently observed in those of advancing years; such a tongue is not indicative of pernicious anemia

As the result of the anemia a fever, temperature up to 100 F, may occur which disappears promptly after effective treatment

Cardiac murmurs are often heard and occasionally there is a diastolic murmur at the aortic area. The vessels in the neck pulsate if the anemia is severe, and venous hums may be present. The blood pressure is commonly low in pernicious anemia

The liver is often detectably enlarged. When there is congestive heart failure in association with the anemia, the liver may be greatly enlarged and tender. The spleen is moderately increased in size before treatment and during relapses A very large spleen is unusual. With adequate treatment the liver and spleen return to their normal sizes

Significant findings on examination are bilateral diminution or loss of vibratory sensation over the tibias and bones of the arms and in-co-ordination in the lower extremities In-co-ordination, resulting in disturbance of gait, may be more severe on one side than on the other The fingers often lose the power to perform synchronized movements. These signs indicate a combined sclerosis of both the posterior and the lateral funiculi and involvement of peripheral nerves. The peripheral nerve degeneration accounts for the hyperesthesia of the soles of the feet

Examination of the blood reveals macrocytes filled with hemoglobin, irrespective of size and shape, which are characteristic of pernicious anemia The greater the anemia, the more macrocytes are present in the blood. The macrocytes may be circular or oval and may have a diffuse basophilia

In the blood of those who have advanced pernicious anemia all the abnormalities of prematurity of erythrocytes except hypochromia may be present There may be a punctate basophilia, chromatin particles (Howell-Jolly bodies), acidophilic rings of various shapes (Cabot's rings), and nucleated erythrocytes The cytoplasm of the nucleated erythrocytes may be acidophilic, polychromatic or basophilic.

The erythrocytic diameters are estimated by the *mean corpuscular volume.* When the anemia is slight or moderate, values of 95 to 110 cubic microns are common (normal 82 to 92 cubic microns). When the anemia is more severe, the mean corpuscular volume may reach 150 cubic microns. The volume index and the color index are increased.

The erythrocytes in pernicious anemia are not supersaturated with hemoglobin The increased corpuscular size accounts for the increased amount of hemoglobin in pernicious anemia The erythrocyte count is often found to be lower than the appearance of the patient suggests

The *iron content of the serum* is abnormally high. The blood *plasma* is yellow in pernicious anemia The van den Bergh reaction is indirect and the quantity of serum bilirubin is increased, owing to hemolysis, which is characteristic of the disease

Achlorhydria is present. The diagnosis of pernicious anemia should not be made unless there is achlorhydria manifested by a *failure to secrete free hydrochloric acid* after ingestion of a test meal, or even after the subcutaneous injection of histamine (0 005 mg per kilogram of body weight).

During relapse the urobilinogen and urobilin are increased in the *urine* to several times their normal values

The leukocyte count is often low, and there may be relative lymphocytosis and hypersegmented neutrophilic leukocytes. Eosinophilia may be present.

DIAGNOSIS A sore tongue, numbness, tingling, and weakness of the legs, associated with the presence of a macrocytic anemia and achlorhydria, are diagnostic.

If a macrocytic anemia is revealed, it will then be realized that the color index is increased. The smear may reveal large, well-filled red corpuscles and misshapen red cells (poikilocytosis), a punctate basophilia (Howell-Jolly bodies), or rings (Cabot's rings), and occasionally nucleated erythrocytes (macroblasts and megaloblasts). If a competent cytologist does not see the blood smears, and free hydrochloric acid is absent from the gastric contents, a therapeutic test by administration of liver extract may be diagnostically useful A favorable response favors the diagnosis of pernicious anemia but is not conclusive. The administration of a potent liver extract, if the patient has pernicious anemia, is followed in several days by a characteristic reticulocyte response and rapid relief of symptoms, as well as a rise in the erythrocyte count unless there is some complicating disease. If the parenteral administration of a liver extract of known potency is not followed within 10 to 14 days by definite signs of response, the diagnosis of pernicious anemia must not be made. It may be impossible to make a diagnosis of pernicious anemia in patients who fail to respond to treatment, or in patients who have received treatment. The only time a definite diagnosis can be made after a patient who has received liver for the treatment of pernicious anemia has not responded is when there is free hydrochloric acid in the gastric contents. If there is free hydrochloric acid in the gastric contents, the patient does not have and did not have pernicious anemia

In those who have crippling neurologic disorders (a combined sclerosis) and secondary infection, death is not preventable. In all others the prognosis is good if adequate liver therapy is maintained

Macrocytic Anemia Associated With Sprue, Nontropical Sprue, Idiopathic Steatorrhea and Celiac Disease. These conditions are all considered in Chapter 22

Macrocytic Anemia and Digestive Disease. A macrocytic anemia may occur in those having carcinoma or polyposis of the stomach who do not have pernicious anemia It may occur after partial gastrectomy In relation to the number of such operations which have been performed, the incidence of macrocytic anemia following these operations is small Hypochromic anemia is of common occurrence in gastrectomized individuals

Patients who have intestinal strictures and enteroenterostomies, gastroenterostomies, enterocolostomies, or gastrojejunocolic fistula or gastrocolic fistula and extensive ileitis, may have macrocytic anemia

Progressive weakness and loss of weight are always present and a few patients have glossitis However, manifestations of disease of the nervous system similar to those present in pernicious anemia are absent in these intestinal macrocytic anemias

The physical examination reveals loss of weight, weakness and often tenderness of the abdomen Examination of the blood reveals findings seemingly identical with those of pernicious anemia in regard both to morphology and to degree of reduction in the erythrocyte count In one half of these patients analysis of gastric *contents* reveals free hydrochloric acid, a finding which immediately eliminates pernicious anemia

Macrocytic Anemia in Diseases of the Liver. *Macrocytic* anemia may be associated with disease of the liver. The anemia resembles that seen in pernicious anemia although it is rarely as severe.

In severe hepatic disease the macrocytic anemia may be the result of defective storage or metabolism of the *antianemic principle*. In a patient who has hepatic disease which may accompany chronic alcoholism, the macrocytic anemia may be

the result of a dietary deficiency state, for in some chronic alcoholics faulty absorption is evident. In others increased destruction of blood is etiologically obvious and important.

Infestation With Diphyllobothrium latum (Fish Tapeworm) It has been said that persons infested with fish tapeworm (*Diphyllobothrium latum*) may have signs and symptoms resembling in all respects those of pernicious anemia, including such symptoms as glossitis, diarrhea, paresthesias and ataxia, as well as the classic blood findings

Macrocytic anemia is rarely encountered, however, when there is infestation with the fish tapeworm The evidence strongly suggests that anemia in association with fish tapeworm infestation is in many instances a matter of coincidence. In cases in which the anemia is relieved after removal of the parasite it is possible that the tapeworm acts in some way to precipitate anemia in a constitutionally predisposed individual.

Macrocytic Anemia and Endocrine Disease. A yellowish pallor of the skin associated with anemia is common in hypothyroidism The anemia of myxedema is rarely severe and is usually normocytic or macrocytic, or it may be hypochromic. Pernicious anemia and myxedema may occur in the same individual, and the presence of hypothyroidism may inhibit the response to liver therapy. The erythrocytes are uniformly larger than normal cells. There is no poikilocytosis or evidence of active blood regeneration. The administration of thyroid is followed by a very slow restoration of the blood to normal

Achrestic Anemia. Achrestic anemia is a rare form of macrocytic anemia which is characterized by a chronic but progressive and often fatal course, and responds temporarily, or not at all, to liver therapy. The morbid anatomy resembles that of pernicious anemia

MICROCYTIC ANEMIA

(Iron Deficiency Anemia)

This type of anemia is known also as nutritional hypochromic anemia, chronic or idiopathic hypochromic anemia, and chlorosis

The term hypochromic indicates that the concentration of hemoglobin of the erythrocytes is quantitatively reduced, both from the reduced size of the cell and *from the reduced amount of hemoglobin contained therein* The concentration of iron in the serum is decreased in iron deficiency anemia. The term hypochromic microcytic anemia indicates iron deficiency except when the patient has Mediterranean anemia

The causative factors operative in the production of iron deficiency are chronic loss of blood, disorders of the alimentary tract which may be due to an inadequate diet, or the result of chronic diarrhea, hookworm disease or perhaps achlorhydria

Hypochromic anemia is observed in association with bleeding from the uterus (menorrhagia and metrorrhagia), peptic ulcer, bleeding hemorrhoids, carcinoma of the stomach or colon, ulcerative colitis or ileitis, bleeding varices and severe epistaxis or repeated hemoptysis It is frequently seen in multiple hereditary telangiectasia and may be found in chronic thrombocytopenic purpura Iron deficiency anemia occurs most frequently in women

Chlorosis. The name chlorosis formerly was used to designate the anemia of young women. The term arose from the greenish yellow color of the affected girls Anemia occurring in girls and young women, when it results from dietary deficiencies, is usually mild If it is accompanied by menorrhagia, it may be severe

There is a chronic microcytic anemia which occurs in women in the third to fifth decades of life which is similar in many respects to chlorosis This anemia has been ... *chlorosis*, and essential,

... is, for in a family there

may have been hypochromic microcytic anemia in the women, and one or more of the men of the family may have had pernicious anemia

Hypochromic microcytic anemia more frequently affects white persons, but it is observed in Negroes. In many instances it is associated with achlorhydria and it is more common and more pronounced in the poor than in the prosperous

The history almost always includes rapidly repeated gestation with excessive loss of blood, an inadequate convalescence following illnesses or gestation, or both Menstrual disturbances, often menorrhagia, are common

Many women who have hypochromic anemia in pregnancy are found to have been anemic before. The hydremia of pregnancy often accentuates an already existent anemia

SYMPTOMS. The first symptoms are weakness, fatigability, and often pallor. The nervous irritability, inability of mental effort, headache, dyspareunia, and disturbances of sleep do not arise from the effects of the anemia Likewise the anemia cannot be held responsible for the lack of attraction which these women have for members of the male sex

The judgment and appetite are capricious, manifested by abnormal cravings for unusual articles of food Aerophagia, heartburn and epigastric distress are common, but no commoner than constipation or diarrhea Difficulty in swallowing, *sore tongue, or sore mouth*, is often present

Palpitation, dyspnea on exertion, and choking sensations and inability to take a deep breath are common complaints Sighing respirations may be an objective symptom. Starting on beginning to sleep is common and may be interpreted by some of these women as heart trouble

Neuromuscular pains, vasomotor disturbances, numbness and tingling are common in those who have an iron deficiency anemia, but these complaints cannot be considered peculiar to anemia of this kind

EXAMINATION Many of these women are carefully and attractively dressed and through make-up attain the appearance of good physical health They are often gracious and gentle in social intercourse A few are pale, tired and lifeless. The mucous membranes, nail beds and conjunctivae may be pale The skin over the body may be inelastic and dry The skin of the face and hands has a softness and an elastic appearance purely from the effects of cold creams and olive oil The hair is dead in appearance and is often scanty A greenish yellow tint to the skin described by early physicians is rarely observed nowadays. This skin coloration is more commonly seen in young men at the present time and in them it is of a hereditary origin

Papillary atrophy of the tongue may be present Comparable degrees of papillary atrophy, however, occur in those who are not anemic These patients have, and often complain of, a dry mouth Probably as the result of dryness, from a lack of desire for water, fissures occur at the angles of the mouth, and on the mucous membranes of the mouth are often small bullae surrounded by areas of erythema

Functional systolic cardiac murmurs are common The abdominal wall is atonic and inelastic The liver is often palpable, the spleen rarely so

In the blood there are microcytes and elongated poikilocytes. There may be some macrocytes and polychromatophils, which indicate a feeble effort to form hemoglobin-containing corpuscles Reticulocytes are normal and an occasional normoblast and microblast may be found. The hemoglobin is reduced out of proportion to the erythrocyte count and volume of packed red cells The erythrocyte count may be normal or even somewhat above normal when the hemoglobin is as low as 8 gm per 100 ml. of blood The platelets are usually normal in number and small The plasma protein content is often reduced. The leukocytes may be normal in number or slightly reduced Achlorhydria is a common finding. The bone marrow is hyperplastic and shows a relative as well as an absolute increase of normoblasts

DIAGNOSIS The diagnosis of hypochromic anemia is made by those who are accustomed to examining stained blood smears and is based on the presence of

decreased hemoglobin concentration and a decrease in the volume of the packed cells. In many instances it will be observed that the etiologic factors operating in the production of hypochromic microcytic anemia are apparently the same as those present in the production of a hyperchromic macrocytic anemia.

Relapses occur unless administration of iron is continued. This is true particularly in women before the climacteric.

The iron deficiency disease, *kasai*, occurs in the dark-skinned natives of tropical climates This is the same condition as the hypochromic microcytic anemia of the white races It is characterized by anemia, edema, digestive disturbances, and depigmentation of the skin However, the common form of depigmentation of the skin, vitiligo, is not due to an anemia (see Chapter 8)

POLYCYTHEMIA

Increases in the number of erythrocytes (more than 5,500,000 cells per cubic millimeter) may be absolute or permanent, as in polycythemia vera, or the increases may be relative or transient or permanent as in conditions of anoxia In either instance the increase in erythrocytes is termed erythremia or polycythemia.

Polycythemia Vera (Erythremia, Absolute Polycythemia) This disease is designated most commonly, in addition to the foregoing names, as Vaquez' disease, Osler's disease, polycythemia rubra, and cryptogenic polycythemia

The terms Gaisbock's syndrome and polycythemia hypertonica refer to the occurrence of polycythemia and hypertension without splenomegaly. In this condition there is moderate or marked arteriosclerosis and the heart is enlarged Apoplectic strokes are common. There is no good reason for distinguishing this syndrome.

The disease is said to be most frequent in Jews and rare in Negroes Some have thought that polycythemia vera or erythremia may have a familial tendency. The cause is unknown The age at onset of symptoms in most cases is in middle or late life

PATHOLOGY The spleen is enlarged, smooth, moderately hard, and may contain infarcts, thrombi and cysts The liver is often enlarged, hyperemic, and may be cirrhotic The bone marrow shows evidence of active hematopoiesis The blood flow is slowed as the result of increased viscosity of the blood and thus infarcts and thrombi are commonly present.

SYMPTOMS. The usual experience is that there are no symptoms which can be attributed to polycythemia. The symptoms are the common ones of weakness, headache, dizziness, ringing in the ears, and visual disturbances In the more advanced instances of the disease dyspnea and weakness are the chief complaints. Headache is a common complaint Vertigo and giddiness, transitory syncope, insomnia, weakness, a sensation of fullness in the head, and numbness and tingling in the fingers and in the feet are very common

Visual disturbances, including dimness of vision, sometimes temporary blindness, scotomata, specks and bright points in the field of vision, diplopia and temporary paralysis of one of the eye muscles, are frequent complaints All visual disturbances are usually increased on raising the head from a lowered position

Intercurrent infections are frequent, especially those of the respiratory tract Bronchitis and emphysema may develop In patients who have hypertension, particularly, chronic renal disease and arteriosclerosis are common

As the disease progresses, epistaxis, bleeding gums, and massive hemorrhages from varices in the esophagus, stomach or bowel, and respiratory passages, and hemorrhage into the peritoneal cavity and into the spleen may appear suddenly Thrombi in the mesenteric veins and arteries are not diagnosable as such. When thrombosis occurs, the symptoms are very much like those of a general peritonitis or the perforation of an ulcer. Dyspnea on exertion, cough and hoarseness are usual Respiratory infections are easily acquired by these patients.

Vascular lesions of the brain of sudden onset constitute the most frequent and

serious complication A paralysis may be the first symptom, less common are myoclonia, chorea, attacks of grand mal, and symptoms suggesting brain tumor, general paresis and tabes. Narcolepsy, attacks of catalepsy, and psychic disturbances of various types, including loss of memory, mental depression, confusion, hallucinations, and slurring of speech, may be associated with and caused by a polycythemia vera.

Pains in the legs are troublesome and severe Paresthesias and pruritus may be very troublesome Swelling and pain (erythromelalgia) in the extremities are common. Thrombosis is a common occurrence in arteries in every part of the body in polycythemia. The symptoms from the various and widely distributed thrombi may be perplexing

EXAMINATION. The color of the face, particularly of the lips, cheeks, tip of the nose, the ears, the neck, and also of the distal portions of the extremities, produces the characteristic appearance (rubor) of these patients The degree of red or blue and the sensitiveness to cold of the skin depend on the quantity of reduced hemoglobin present and thus on the severity of the disease.

Ecchymoses of various sizes are common, manifested as red or dark violet spots, or brownish pigmentation of the skin and mucous membranes. Hematomas may occur in any part of the body, and they are often present in the urinary bladder, vagina and perineal regions and cause pain on sitting and on urination Descriptions of the varied skin lesions include dry skin, eczema, acneform or urticarial changes, acne rosacea and even a nodular eruption similar to the specific infiltration found in leukemia.

The peripheral arteries are often markedly thickened The changes in these arteries may reproduce the findings present in an atherosclerosis in the peripheral vessels. Vascular accidents, coronary thrombosis, claudication without occlusion, arterial occlusion with gangrene, acroparesthesia, the Raynaud phenomenon and thromboangiitis obliterans may be present Venous thrombosis, varicosities and phlebitis are commonly found The heart is enlarged Coronary occlusions and cerebral vascular accidents are common

Enlargement of the liver is the rule Cirrhosis of the liver may be an accompaniment Splenomegaly is present in 9 of every 10 cases The spleen may vary greatly in size, and in rare instances it may even extend to the pelvis Sudden pain in the splenic region followed by a friction rub is indicative of infarction

The mucous membranes of the eyes appear congested, cyanotic, or even bloodshot. On examination of the eyegrounds the vessels are observed to be engorged, tortuous and irregular in diameter, the veins are dark and the retina is deeply colored Papilledema and embolism of the central retinal artery may occasionally be found.

On examination of the blood, erythrocyte counts of 6,000,000 to 10,000,000, or 12,000,000 per cubic millimeter are common In instances of marked polycythemia the mean corpuscular volume is reduced below normal Hemoglobin values of 17 to 24 gm per 100 ml accompany the polycythemia However, the hemoglobin may [illegible] mean corp[illegible] may be re[illegible] with polyc[illegible],000 or 40,000 or higher, the increase is in the myeloid leukocytes and the metamyelocytes. The blood platelets are increased to 1,000,000 to 2,000,000 per cubic millimeter The clot retracts poorly The viscosity of the blood may be *5 to 8 times* greater than normal The specific gravity is 1 075 to 1 080, as compared with 1 052 to 1 063 normally. The viscosity and specific gravity of the serum are less than is normal The sedimentation rate of polycythemic blood is delayed. The hematocrit percentage is markedly elevated The reading is found to be 60 or higher

in many of these patients. This increase in the hematocrit is in accord with high specific gravity and greater viscosity of the blood. The total blood volume is increased It may be as great at 121 to 246 ml. per kilogram of body weight, as compared with the normal mean volume of 87 ml. The plasma volume is not increased

The basal metabolic rate may be increased in some

The findings on analysis of the urine are not significant

DIAGNOSIS. The presence of cyanosis, splenomegaly, polycythemia, polychromatophilia, leukocytosis, and thrombocytosis usually suffices for a diagnosis of polycythemia vera. An increased total blood volume and an increased hematocrit are important diagnostic assurances Polycythemia vera is differentiated from a secondary polycythemia by the absence of chronic cardiac or pulmonary disease in those living at an altitude of less than one mile

The course may be chronic and 10 to 15 years or more in duration without serious complications In some the disease seems to remain stationary for years However, serious symptoms may develop at any time. The most serious development, which may cause sudden death, is occlusion of the coronary or cerebral arteries.

Relative and Transient Polycythemias. The causes for a *transient polycythemia* are more numerous and varied than those of *relative polycythemia* but usually find their origin in disease of the heart or lungs The commonest cause of a relative polycythemia is dehydration The total blood volume is reduced in relative polycythemia owing to the decrease in plasma volume, whereas in *absolute polycythemia* the total blood volume is normal or increased. Transient polycythemia occurs when there is a mixing and shunting of even small amounts of blood from the pulmonary circuit. The common defects producing such shunting of blood are pulmonary stenosis, usually with defective ventricular or auricular septum, patent foramen ovale or patent ductus arteriosus; persistent truncus arteriosus; complete transposition of arterial trunks; and the tetralogy of Fallot. These patients are markedly cyanotic. They have clubbing of the fingers and toes, and sometimes stunted growth since the heart lesions are of congenital origin

Polycythemia of mild degree occurs in some acquired heart disease such as mitral stenosis when there is anoxemia as the result of decreased cardiac reserve with an impaired systemic circulation and changes in the pulmonary tissues

Emphysema is the common chronic pulmonary condition which produces cyanosis and in time polycythemia. Silicosis, cavernous pulmonary hemangioma and pulmonary arteriovenous fistula are associated with polycythemia, cyanosis, hemoptysis and clubbing of the fingers

Exposure to high altitudes may be accompanied by acute symptoms of fatigue, dizziness, headache, nausea, ringing in the ears, and occasionally vomiting, chills, and prostration When adaptation occurs, the symptoms disappear with a regular appearance of polycythemia. Some individuals, however, even though they are acclimatized to high altitudes, may suffer from an insidious disorder known as *chronic mountain sickness* (Monge's disease) In chronic mountain sickness a state of tissue anoxemia may develop

Those affected by chronic altitude sickness are usually in the fourth to sixth decades of life Monge described (1) an emphysematous type and (2) an erythremic type.

In the *emphysematous type* there are chronic dyspnea, frequent bronchitis, laryngitis and cyanosis. There is a symptomatic improvement on residence at lower altitudes. In the *erythremic type* there are a reduction in mental and physical fitness, occipital headache, and an erythremic color of the face while at rest. On exertion the face is cyanotic. Epistaxis, nausea, vomiting, diminution of vision, and paresthesias may ensue if exertion is not stopped The disorder may progress, irrespective of exertion, to aphonia (aphonia of dyspnea), lethargy, and coma The

skin and scleras are deeply colored, the tongue is thickened, the hands are enlarged, and the fingers are clubbed

On examination it may be impossible to determine whether or not there is left-sided heart failure. Polycythemia is present, and it is more marked than in the other residents at the same altitude who do not have symptoms. Cell counts of 7,000,000 to 9,000,000 per cubic millimeter of blood are common There is a corresponding rise in hemoglobin and volume of packed red cells The blood volume is increased The van den Bergh reaction is indirect, and the concentration of bilirubin is increased.

Descent to sea level brings about complete relief of symptoms and thus establishes the diagnosis

Polycythemia may be associated with the presence of subtentorial tumors and Cushing's disease and Cushing's syndrome

Chronic poisoning by coal-tar derivatives, anilin and its derivatives, gum shellac, phosphorus, and metals, such as manganese, mercury, iron, bismuth subnitrate, arsenicals and cobalt, may produce polycythemia (see Chemical Agents, Chapter 19).

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13

DISEASES OF THE ESOPHAGUS, ABDOMINAL WALL AND ABDOMINAL CONTENTS EXCLUSIVE OF THE ENDOCRINE GLANDS, SPLEEN AND GENITOURINARY TRACT

MANIFESTATIONS OF DIGESTIVE DISEASE

Anorexia. The term anorexia refers to the lack or loss of appetite for food. Anorexia is caused by organic disease, by functional disorders, and by many chronic wasting diseases attended by pain The commonest of all causes for anorexia is fever.

One type of primary anorexia, anorexia nervosa, has been described as a clinical entity Berkman summarized the sequence of events in anorexia nervosa as follows: Usually a primary psychic disturbance is obvious and seems to be directly responsible for the loss of appetite The reduction in the intake of food leads to inanition, which is associated with a lowering of the metabolic rate. The lowered metabolic rate means reduced food requirements Most of the weight is lost during the early part of the disease Sooner or later the weight becomes more stationary. This lowering in the rate of metabolism may be looked upon as a protective mechanism.

The clinical features of anorexia nervosa are a primary loss of appetite with an actual revulsion against food, often associated with vomiting after the taking of food, and marked loss in weight with surprisingly little loss in strength for a long period of time Amenorrhea is frequent

Physical examination often reveals a dry parched skin with bruise marks and eczema A brownish pigmentation may be present In many patients the extremities are cold and blue The temperature may be subnormal, the pulse slow and the systolic blood pressure low. The basal metabolic rate is almost universally −15 to −25 per cent

The ailment may prove to be extremely serious and in an occasional case may be fatal, as the result of exhaustion, pneumonia, or some other secondary infection. The diagnosis can be made only after the possibility of existing organic disease has been eliminated

Abdominal Pain. The mechanisms of abdominal pain are not well known However, abdominal pain can arise (1) in the viscera, when it is known as pain of visceral origin, (2) in the parietes or (3) in a viscus from which it is referred to a distant part (referred pain; see Chapter 2).

Visceral Pain. True visceral pain is produced by increased intravisceral pressure as the result of failure of relaxation or distention of the visceral musculature. This type [illegible] ossibly as a cramplike sensation [illegible] instances it may be relieved by [illegible] in intravisceral pressure, or by the development of gangrene

Pain provoked by obstruction to the bowel, spasm of the bile duct or ureter or blood vessels, the initial pain of acute appendicitis and of acute cholecystitis, and the pain which is present in some instances of ulcer with its associated pylorospasm, gastrospasm, or cardiospasm, are examples of true visceral pain

diseases of the nervous system, particularly neurasthenia, psychoneurosis, psychosis, brain tumor and cerebrospinal syphilis.

Parorexia. Parorexia denotes an appetite for unusual foods or a perversion of normal appetite. It is not concerned with the mechanism of hunger. In some instances, it may be a desire for spices, highly seasoned food or acid foods. Parorexia usually is associated with a psychoneurosis or a psychosis. In patients in the latter group actual depravities in appetite may develop. This is pica, a desire for ingesting things other than food In certain of the psychoses pica may change to allotriophagy, a desire for offensive food

Dysphagia. Dysphagia may be produced by anything which interferes with the normal act of deglutition in the mouth, the upper part of the respiratory passage, or the pharynx, or in the cervical portion of the esophagus, the midesophagus, or the lower 2 or 3 inches of the esophagus.

Lesions of the mouth or the tongue which are painful may cause dysphagia. In affections of the pharynx and larynx difficulty in deglutition occurs synchronously with the passage of the bolus from the mouth into the pharynx and upper part of the esophagus The pharyngeal and laryngeal affections which interfere with swallowing include acute or chronic infections, retropharyngeal abscess, and paralysis. The bulbar type of syringomyelia, strokes, and other bulbar lesions may cause weakness of the pharynx and loss of power to swallow. Myasthenia gravis may act in this way. If abnormal deglutition is associated with strangulation, coughing, or nasal regurgitation, central lesions of the bulbar type, myasthenia gravis, or diseases irritating the ninth or tenth cranial nerves are usually present A fistulous communication between the esophagus and the trachea or a bronchus may cause dysphagia, strangulation and coughing Malignant disease of the epiglottis or the arytenoid cartilages and pharyngeal pouches may cause dysphagia

Dysphagia occurring from 2 to 5 seconds after swallowing is caused by disorders of the proximal portion of the esophagus. Dysphagia occurs frequently as a symptom of lesions of the middle portion of the esophagus

Discomfort in the region of the ensiform cartilage, coming on from 5 to 15 seconds after swallowing, is suggestive of disease in the lower portion of the esophagus Diseases of the cardiac end of the stomach and hiatal hernia may cause dysphagia

Regurgitation and Rumination. *Regurgitation* is the ejection of chyme or gastric juice into the mouth It is distinguished from vomiting by the small quantities of material ejected and by lack of the participation of the action of the accessory muscles (diaphragm and thoracic muscles) which serve in vomiting

When food is regurgitated into the mouth, if it is chewed and swallowed again, these acts comprise the phenomenon of *rumination*. The term is also used to describe the act of regurgitating food back into the mouth and reswallowing it rather than expectorating it. The mechanism and clinical significance of rumination are similar to those of regurgitation except that the food has not been expelled, because it is not disagreeable to the taste and more often because the act of expelling it is not condoned by custom Rumination is an infrequent and an unimportant symptom However, it may occur in more than one member of a family

Sitophobia. The term sitophobia is used to describe a fear of eating because of painful sensations which have occurred after eating. Sitophobia is frequently a manifestation of anxiety, although it may be due to organic disease in the esophagus or the stomach causing distress after the ingestion of food

Belching, Aerophagia and Pneumatosis. A small gas bubble or "magenblase" is present in the normal stomach, and in the absence of any physiologic derangement the eructation or belching of gas may occur from the stomach once or twice after a large meal.

Air residing in the mouth and pharynx may remain in the lower part of the

esophagus The patient learns to bring it up voluntarily with a loud report. At times, without bringing the air up, the patient continues to reswallow, so that an increased amount of air accumulates in the stomach. After swallowed air enters the stomach, it is not always possible to eructate it voluntarily. Involuntary eructation of gas commonly is associated with the act of *aerophagia*

The neurotic person in whom aerophagia and belching develop likes to put on the act before an audience, hoping to impress his family or the physician with the seriousness of the complaint. The habit may be formed by patients who are not psychoneurotic In the latter it is easily corrected by an explanation of the harmful effect. These patients are instructed to open the mouth when there is a desire to eructate The treatment of the psychoneurotic aerophagic is disappointing.

The term *pneumatosis* often is used to describe attacks of gastric distension, dyspnea, or precordial oppression due to pressure by the stomach, inflated with excessive air, on the left leaflet of the diaphragm. The symptoms complained of are shortness of breath, a smothering sensation, cardiac pain, palpitation and sometimes a fear of impending death The syndrome attends aerophagia

Borborygmus. Borborygmus is defined as a gurgling of fluid and gas in the intestine due to peristaltic activity It may be the initial complaint in beginning obstruction of the intestinal tract from any cause In other cases, the gurgling sounds may depend on intestinal hypermotility attending emotional tension and aerophagia.

Borborygmus is a frequent complaint of asthenic, splanchnoptotic, underweight women At times the noises produced by peristaltic activity in these patients may be heard some distance away from them. Unless the symptom is of recent origin it is not often of serious importance to anyone except the psychoneurotic patient.

Expulsion of Flatus. An occasional expulsion of flatus is a normal phenomenon Beazel and Ivy measured the colonic flatus egested in 24 hours by 5 "normal" ambulatory students and found the mean average quantity to be 527 ml. These subjects were unaware of intestinal gas and they were not conscious of passing gas at the time of stool Evidently patients who consciously expel flatus must harbor large amounts of gas in the colon, for normally gas sufficient to give rise to the conscious expulsion of flatus, except during the act of defecation, does not reside in the distal portion of the colon

Flatus is associated with constipation. Often air is introduced by laxatives and enemas used in the treatment of constipation. Increased amounts of intestinal flatus attend poorly balanced diets, particularly the ingestion of excessive quantities of cellulose, beans or other legumes Food incompatibility or idiosyncrasy may give rise to excessive gas in the colon Flatus is present in diseases accompanied by defective intestinal absorption such as steatorrhea, sprue, regional enteritis, nutritional deficiency states, and occasionally after ingestion of excessive carbohydrates.

A Sense of Fullness. A feeling of fullness or gaseous distension is often complained of by those who have diverse digestive disturbances This sense of fullness may not be easily differentiated from a feeling of early satiety experienced after the eating of only a small amount of food Usually the latter symptom is of serious import, if the food intake becomes progressively decreased

Any abdominal lesion capable of producing pain may be associated with a vague sense of fullness or pressure rather than pain if the stimulus arising from the lesion is inadequate or if the pain threshold is high

A feeling of fullness or pressure situated in the epigastrium is most frequently of functional origin Air swallowing, the bolting of food, overeating and eating when fatigued or nervously overwrought are the commonest causes

Hematemesis and Melena. The term hematemesis refers to the vomiting of blood, whereas hemoptysis refers to the spitting of blood

The term melena refers to the passage of black tarry feces, usually resulting from hemorrhage into the upper part of the alimentary canal The causes for hem-

atemesis and for melena are often the same, and therefore in this discussion the two conditions will be considered together.

The quantity of blood required for the production of melena must vary Perhaps 2 fluid ounces (about 60 ml) of blood, free in the upper part of the intestinal tract, if passed quickly along the intestine, could cause a tarry stool. If there is not a quickened passage of blood through the small intestine, a larger amount of blood is required before a tarry stool is produced. *Not all black or tarry stools are due to the passage of blood* Melena may be simulated by alterations in the color of the feces following the ingestion of iron, charcoal, bismuth, neoprontosil, beets, blueberries, spinach, and other foods and drinks.

CAUSES. In order to enumerate, the following list is given which is the classification of melena by Balfour as modified by Bockus

A *Intragastric and Duodenal Causes* (1) Peptic ulcer (including duodenal and postoperative ulcers), (2) gastritis and duodenitis (erosions), (3) gastric malignant disease; (4) syphilis and tuberculosis of the stomach, (5) benign tumor of the stomach or duodenum; (6) postoperative hemorrhage; (7) rupture of a sclerotic blood vessel, (8) gastric crisis of tabes dorsalis; (9) supradiaphragmatic stomach (hiatus hernia) and (10) trauma

B. *Extragastric and Extraduodenal Causes* (1) Cirrhosis of the liver; (2) portal or mesenteric thrombosis (portal hypertension due to other causes); (3) splenic diseases. splenic anemia, Banti's syndrome (congestive splenomegaly, and other types of splenomegaly), (4) diseases of the esophagus: malignant or benign tumor, peptic ulcer, esophagitis and erosions, syphilis, tuberculosis and actinomycosis, diverticula and foreign body, (5) blood diseases purpura, polycythemia, hemophilia, pseudohemophilia or fibrinopenia, hereditary hemorrhagic angiomatosis, hemorrhagic disease of the newborn, pernicious anemia, hemolytic jaundice, Hodgkin's disease, and leukemia; (6) jaundice (prothrombin deficiency), (7) diseases of gallbladder, appendix and pancreas (carcinoma of pancreas involving the duodenum, gallstone or malignant lesion eroding into the stomach or duodenum), (8) lesions of the small intestine. benign and malignant tumors, carcinoma of the papilla of Vater, (9) cardiac and pulmonary disease, (10) other systemic causes (toxic, infectious and nutritional conditions and shock); (11) aneurysm or abscess ruptured into the gastrointestinal tract, (12) swallowed blood. epistaxis, hemoptysis, bleeding from mouth and pharynx, and malingering, (13) vicarious menstruation and (14) bleeding internal hemorrhoids, fissures and rectal polyps.

This is a long list of diseases and conditions which may cause intestinal bleeding, many of which will never be observed during a lifetime of the practice of medicine The commoner causes only will be considered here The uncommon causes are considered in association with primary diseases of which they are a part.

Intragastric and Duodenal Causes In the series of hematemesis and melena recorded by Rivers and Wilbur 9 of every 10 patients had *peptic ulcer* Three of every 10 patients who have hematemesis or melena are in the fifth decade of life and 7 of every 10 are men

Rivers and Wilbur observed that hemorrhage often occurs from small congested vessels surrounding the ulcerated region or from vessels in the buds of vascular granulation tissue in the base of a peptic ulcer If one of these buds breaks off, profuse *bleeding is postulated Neither the size of the* ulcer nor the size of the bleeding vessels may have anything to do with the magnitude of the hemorrhage.

Pain is not thought of as a symptom of melena, but if pain is present and if it persists after a severe hemorrhage from a peptic ulcer it often indicates a continuation of bleeding and a luck of ulcer healing There are *no criteria* which, when followed, will establish the exact cause and site of the bleeding The hemorrhage on occasion may be due to ulcerations or erosions of hypertrophic gastritis or to

[illegible] —ntoms

denitis in many of the elderly patients

Cancer of the stomach, gastric syphilis and tuberculosis, benign tumors of the stomach, gastric crisis of syphilis, supradiaphragmatic stomach (hiatus hernia), trauma and extragastric causes must be included among the less common causes of massive hemorrhage.

Extragastric and Extraduodenal Causes. The extragastric and extraduodenal sources of bleeding are variable and often require extensive investigations to distinguish them one from another In a few cases the source of bleeding is never determined

Massive hematemesis or melena is seldom due to intrinsic disease of the esophagus Carcinoma, the commonest organic disease of the esophagus, is rarely complicated by severe hematemesis Among the very rare esophageal causes of hematemesis may be included congenital nevi, acute and chronic esophagitis, foreign body, diverticulitis, syphilis, tuberculosis, and actinomycosis of the esophagus

The pathologic conditions of the small intestine which cause hemorrhage and melena are acute enteritis and chronic enteritis Regional involvement of the various segments of the small intestine, particularly the terminal portion of the ileum by regional enteritis is not a common cause of large hemorrhages, but slow bleeding occurs in this disease Benign ulcer of the ileum with or without ectopic tissue may cause hemorrhage Meckel's diverticulum containing ectopic tissue (often gastric) may cause massive hemorrhages Benign and malignant polyps or any sort of malignant lesions cause bleeding in some instances Diverticula of the small intestine are a rare cause of bleeding.

In the colon the common conditions causing melena are bacillary dysentery, idiopathic ulcerative colitis, amebic colitis (occasionally), polyps and carcinoma. Diverticulum of the colon rarely causes bleeding Rectal bleeding in a patient who has diverticulosis is not usually from a diverticulum but often from a polyp which has not been discovered

Melena is most commonly due to hemorrhoids. Usually in hemorrhoidal bleeding the blood is bright red and streaked on the stools or may drip from the anus during defecation In rare instances hemorrhoids may bleed suddenly while the patient is walking The causes of melena of rectal origin are considered with anorectal diseases

The bleeding in cirrhosis of the liver arises from varicose esophageal veins. The hemorrhage in splenic anemia may prove fatal immediately, or repeated bleeding may occur over a period of 10 or 15 years Other types of splenomegaly, not of congestive origin, rarely cause severe hemorrhage Balfour expressed the belief that the bleeding is not mechanical in origin, since hemorrhage is rare in myelogenous leukemia and in hemolytic icterus, conditions characterized by great splenic enlargement

Chronic ulcers and benign or malignant tumors of the mouth, tonsils and pharynx are causes of the swallowing of sufficient blood to produce hematemesis and melena Gingivitis due to scurvy or to the administration of mercury may cause large amounts of blood to be swallowed and subsequently vomited or passed on through the bowel

Massive hemorrhage may occur in any type of jaundice It is exceedingly rare in hemolytic icterus and in hypertrophic biliary cirrhosis and commoner in association with obstructive jaundice

Carcinoma of the papilla of Vater, and isolated primary tumors or ulcers in the small intestine, may be the source of melena. In congestive right-sided heart [illegible] ...ase and, occasionally, in ad- [illegible] ... occur.

[illegible] ...ed with massive bleeding are [illegible] ..., malaria, yellow fever and

Bleeding into the upper part of the gastrointestinal tract, particularly after trauma or operation, may be caused by hemophilia. Only males are hemophilic, but pseudohemophilia affects both sexes and may cause melena and hematemesis associated with cutaneous and mucosal hemorrhages, and greatly delayed bleeding and coagulation times from the lack of fibrinogen (afibrinogenemia). Conditions similar in manifestations to afibrinogenemia are: congenital hypofibrinogenemia and idiopathic hypothrombinemia (see Chapter 12).

Hematemesis, occurring in an adult showing telangiectasis of cutaneous and mucous membranes, particularly on the face, or in the nose, mouth or pharynx, should suggest the possibility of hereditary hemorrhagic angiomatosis somewhere in the digestive tube

Occasionally a fatal gastrointestinal hemorrhage occurs in polycythemia Thrombocytopenic purpura, either of the essential type (Werlhof's disease) or the symptomatic type, may be associated with a massive hemorrhage into the upper part of the gastrointestinal tract Petechiae or ecchymoses often occur in the skin without erythema, swelling or inflammation

In massive hemorrhages a history from the family, usually of a previous episode of hematemesis or melena, points toward the diagnostic probability of peptic ulcer

SYMPTOMS. There is a sudden desire to defecate which is accompanied by weakness, chilliness, pallor and often nausea Syncope may occur during or soon after the act of defecation Vomiting of blood may take place before or after the bowel movement These symptoms may awake the patient from sleep Stoic individuals may not be alarmed over the passage of a tarry or black stool or concerned about the vomiting of blood until they become so weakened that they cannot work. The sight of blood in the vomitus or in the bowel movement, and the weakness, will cause most patients to seek aid immediately.

EXAMINATION. During the time the hemorrhage is in progress the extent of the examinations must be left to the judgment of the examiner The general rule is that only essential examinations and procedures are conducted at this time The patient remains quiet.

If the hemorrhage is massive, there is shock Shock may come immediately after the loss of a large amount of blood or it may not be manifested for several hours

Hyperazotemia may follow a massive hemorrhage into the upper part of the intestinal tract in the absence of decreased renal functional activity, dehydration, starvation, or shock The hyperazotemia is an expression of the amount of blood protein digested and absorbed from the bowel Hyperazotemia of alimentary origin is often associated with fever and toxic symptoms which begin about 2 days after the onset of bleeding if a large amount of blood has remained in the bowel

Hyperazotemia present after gastrointestinal hemorrhage is more frequently due to dehydration resulting in oliguria and anuria When there is a suppression of urinary output there is a decrease in the excretion of urea followed by an increased concentration of urea in the blood Thus the blood urea nitrogen concentration is greater. A hyperazotemia may be due to a renal insufficiency and not be related to the melena In an occasional patient there may be hyperazotemia as the result of a combination of all of these factors, namely, (1) absorption of blood protein and (2) dehydration and absorption of blood protein, plus an impaired renal function.

A failure of the blood urea nitrogen concentration to return to normal may be due to (1) continuation of the renal impairment as a result of the shock and dehydration, (2) continued bleeding or exacerbation of the hemorrhage or (3) impaired renal function due to renal disease The blood urea nitrogen concentration together with the blood count, hematocrit reading, blood pressure and condition of

the circulation is helpful in establishing or disproving the existence of continued bleeding or renewed bleeding. The mortality rate from hemorrhage when the blood urea nitrogen concentration is more than 100 mg per 100 ml, a state which is associated with renal disease and permanent renal insufficiency, is very high

A complete blood count and hemoglobin reading, blood grouping and determination of the Rh factor and concentration of blood urea are performed routinely on patients who have massive hemorrhage. There should be a reduction in the erythrocyte count and hemoglobin concentration and varying degrees of leukocytosis (12,000 or more per cubic millimeter). On rare occasions there is a pronounced leukocytosis

THE ESOPHAGUS

The esophagus is the only organ of the digestive system that is situated within the thorax In its passage through the thoracic cage it may be seriously affected by diseases of the respiratory and vascular organs More particularly, the esophagus is affected by diseases in the mediastinum It therefore has been mentioned from *time to time in the diagnosis of respiratory, cardiovascular and mediastinal* conditions

In looking into the throat through the mouth, the posterior wall of the pharynx is seen at the level of the body of the second cervical vertebra Seven structures open into the pharynx, namely, the two posterior nares, the two eustachian tubes, the mouth, the larynx, and the esophagus The esophagus begins at the lower end and is the posterior outlet of the pharynx.

PAIN The upper portion of the esophagus is supplied by the recurrent laryngeal nerves and the right and left vagus nerves It is the consensus that pain in cardiospasm is conveyed by vagal afferent fibers In the medulla vagus fibers and the sensory nucleus are in close apposition to the descending tract of the trigeminal nerve, which constitutes a possible route for pain referred to the face in esophageal disorders The somatic sensory nerve from the nodose ganglion of the vagus innervates the external auditory canal and constitutes the most logical pathway for the reference of pain to the ear which occasionally is present in diseases of the esophagus

Esophageal pain is dependent on the state of tension of the esophagus The more severe the pain becomes, the wider is its distribution Pain due to disturbances in the upper portion of the esophagus is likely to be situated over the point corresponding to the underlying esophageal lesion Disturbances in the lower portion of the esophagus give rise to a much more diversified distribution

EXAMINATION Palpation of the esophagus is possible only in the neck, usually on the left side, behind the trachea A distinct tumor found here may be a diverticulum distended with food or fluid, or an abscess from caries of the cervical vertebrae

Auscultation of the esophagus is occasionally of some diagnostic value The stethoscope is placed posteriorly just to the left of the spinal column, about the level of the sixth thoracic vertebra, while the patient swallows a mouthful of water. At the instant of swallowing, a sound (deglutitory) is heard, followed in 6 or 7 seconds by an esophageal bruit, a sound like that heard in one's own ears when swallowing saliva Three to 5 seconds later ensues a secondary sound caused either by the fluid entering the stomach or by regurgitation of air bubbles Delayed appearance of the last-mentioned sounds may be present in esophageal obstruction.

Deformities. Deformities of the esophagus arise from diseases due to prenatal influences and acquired disease of postnatal life In any one patient affected by an esophageal deformity it may be impossible to assign proper values to one or the other of these etiologic categories For instance, a considerable degree of stricturing of the esophagus due to prenatal influence may be present and compatible with health If, however, an acquired disease such as esophagitis resulting from an infec-

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tion, a poison, or lodging of a foreign body arises and adds further stricturing, though of a minor degree, invalidism may follow.

Deformities Due to Prenatal Influences. The esophagus may be absent or atretic, that is, represented by a fibrous cord. The atretic process may be segmental. In early embryonic life the esophagus is normally occluded by a process known as epithelial occlusion Thus the atresias of the esophagus are persistent if this normal process of development stops

In an occasional individual the esophagus may be doubled. Doubling may involve a part or the entire esophagus.

There may be a completely developed esophagus which is too long (dolichoesophagus) or too short Minor degrees of enlargement are dilatations The esophagus may be very large in diameter (giant esophagus).

In association with diaphragmatic and other anomalies of the digestive tube, or anomalies elsewhere in the body, the esophagus may participate in various malformations Congenital webs or bands may constitute causes of narrowing of the esophagus Valvular folds in the esophagus at the level of the diaphragmatic hiatus have been described Such anomalies are probably produced by abnormalities of the crura of the diaphragm

Throughout these descriptions it is remembered that in many of the diseases of the esophagus unknown deformities due to prenatal influence may be present and may be adding their bit to the severity of the disease under consideration.

Atresia. Congenital atresia of the esophagus occurs rarely, and then often in association with some other anomaly of the gastrointestinal tract incompatible with life. However, on occasion, there will be seen a young patient who has a partial or a segmental atresia These lesions often are symptomless unless the esophagus is injured by swallowing a caustic substance

Stenosis. Stenosis of the esophagus may be (1) congenital or (2) acquired

Congenital Stenosis. Congenital stenosis may be due to a fibrous narrowing at any level in the esophagus This malformation in infants is much less frequently encountered than is atresia In adulthood mild stenosis of congenital origin may predispose to the lodging of solid objects or the formation of strictures after esophagitis

Ordinarily a history of dysphagia or regurgitation dates from birth, but may be of little consequence until solid food is added to the diet The degree of dilatation of the esophagus above the stricture will depend on the level of the point of narrowing If it is high up, the dilatation may be very slight In the majority of cases the partial obstruction is high up in the esophagus, usually at the cricoid level Roentgenographic examination is diagnostic.

Acquired Stenosis (Esophageal Stricture). An acquired stenosis usually results from the accidental or intentional swallowing of caustic substances such as lye, acids, bichloride of mercury or ammonia These strictures occur most frequently at the crossing of the left bronchus over the esophagus, in the region of the cricopharyngeus muscle, and at the hiatus Acquired stenosis from infections; from peptic ulcer of the lower part of the esophagus, from trauma to the esophagus by swallowed foreign bodies, and from the vomiting of pregnancy is rare. More commonly no etiologic factor can be found

Many patients who have obstruction of the lower part of the esophagus give a history of a slow insidious onset of dysphagia In the presence of negative results of biopsy a definite diagnosis cannot be established until sufficient time has elapsed after dilatation of a stricture to prove with a fair degree of certainty that the stricture is idiopathic and benign and not of malignant nature A slight congenital stenosis may have been present and unnoticed or ignored until obstruction occurred as a [illegible] in the stenotic region of a bolus of food [illegible] lowed, in some patients [illegible] the swallowing function returns to normal for a while. Dysphagia then returns and becomes progressively worse A severe esophageal injury from swallowing of a caustic substance will not be followed by a symptom-free period The rapidity with which dysphagia develops

depends on the extent and the severity of the injury. As the result of acute starvation in advanced obstructions there are rapid loss of body weight and anemia.

Diagnosis. Roentgenologic examination of the esophagus is the first examination routinely performed and is the most important diagnostically. Esophagoscopic examination permits of visualization of stricture and is essential for the establishment of a definite diagnosis and for securing tissue for microscopic study.

The differential diagnosis between benign stricture, cardiospasm and malignant disease can be made only by biopsy Strictures following the swallowing of lye are frequently multiple.

Diverticula. Diverticula of the esophagus occur in elderly men and women. They are designated, in accordance with their anatomic position, as (1) the pharyngo-esophageal, (2) the epibronchial and (3) the epiphrenal or supradiaphragmatic diverticula The hypopharyngeal pouch is rare and when present does not produce digestive symptoms The pharyngo-esophageal diverticulum is described on page 166

Epibronchial Diverticulum (*Traction Diverticulum*) Epibronchial diverticula occur opposite the bifurcation of the trachea or near the left main bronchus, as the result, usually, of tuberculosis of lymph nodes which are adherent to the esophagus. Disease of the vertebrae may give rise to one of these diverticula of traction type. These diverticula rarely exceed 2 cm in diameter, and may fill and empty readily because of wide mouths, absence of necks, and upward pointing of the sac

Traction diverticula seldom cause symptoms Occasionally they perforate and thus cause mediastinal abscess or esophagobronchial fistula If partial obstruction to the esophagus occurs, a pulsion element may cause further development of the pouch and provoke symptoms

Diagnosis is made by roentgenologic examination

Epiphrenal Diverticulum. An epiphrenal diverticulum is situated in the esophagus near the diaphragmatic hiatus It is a true diverticulum of rare occurrence

The cause of this diverticulum is not known Once started, it usually enlarges in a distalward direction toward the right

The symptoms are vague because of coexistent achalasia There are substernal pain, dysphagia, and vomiting of decomposed but not partly digested food. Regurgitation interferes with sleep

The diagnosis is confirmed by roentgenologic examination

Infections of the Esophagus. Esophagitis occurs in both acute and chronic forms The acute types follow acute infectious diseases, the swallowing of a highly caustic or irritating substance, trauma, excessive vomiting or esophageal intubation, as in treatment of intestinal obstruction and after abdominal operation

Acute Esophagitis. A frequent cause nowadays is trauma of intubation, of vomiting or of the two combined One half of those who have acute esophagitis have been subjected to an inlying nasal catheter and this has been associated with vomiting However, the ingestion of corrosive poisons, hot fluids, or foreign bodies, and such infections as pneumonia, diphtheria, smallpox, glanders, actinomycosis, and blastomycosis are causes of acute esophagitis Subsequent to diphtheria there may be paralysis of the esophagus without pain

The frequency of the association of peptic ulcer and acute esophagitis is reputed to be of common occurrence The acute esophagitis present at postmortem examination is believed to be the result of an agonal episode.

The symptoms of acute esophagitis may suggest a gastric disturbance Substernal pain with extension to the throat during and immediately after deglutition, dysphagia, and occasional hematemesis are characteristic.

Diagnosis in the early stages cannot be proved by roentgenologic examination, as a rule, but endoscopic examination can be used with caution and is the only definite means of diagnosis.

Chronic Esophagitis. Chronic esophagitis may be divided into primary esophagitis and esophagitis secondary either to some other esophageal disease or to disease of an adjacent organ.

Primary Chronic Esophagitis. The predisposing cause of primary chronic esophagitis is the ingestion of irritants such as pepper, hot or cold liquids, drugs and, most of all, alcohol

Secondary Chronic Esophagitis. An esophagitis secondary to obstructing lesions in the esophagus such as cancer, ulcer, cardiospasm, benign stenosis and possibly diverticulum is of a chronic type. It is due to stasis of secretions and food proximal to the point of obstruction Diseases of the thorax and mediastinum may cause esophagitis by contiguity, by interference with the blood supply of the esophagus, or by lymphatic spread of infection Chronic tracheobronchitis, mediastinitis and pressure from mediastinal tumors are accompanied by changes in the esophagus and symptoms subsequent thereto (see Mediastinal Tumors, page 577)

Esophagitis may be incident to a chronic passive congestion, as in congestive heart failure, chronic passive congestion of the lungs or the liver or spasm accompanied by gastric antiperistalsis, for instance, peptic esophagitis. Deficiency states may be accompanied by chronic esophagitis.

A diagnosis of a primary or a secondary chronic esophagitis can be established only by an endoscopic examination.

Tuberculosis of the Esophagus. Esophageal tuberculosis develops by an extension of tuberculous ulcerative pharyngitis, by a perforation into the esophagus of a tuberculous bronchial lymph node or by contiguity secondary to vertebral tuberculosis, and owing to a widespread miliary tuberculosis. Tuberculosis of the esophagus occurs from contact, as from the swallowing of infected tuberculous sputum or food, but rarely causes symptoms

Lesions of esophageal tuberculosis may be ulcerative or hyperplastic. The midportion near the bifurcation of the trachea is the site of predilection of tuberculous lesions, though they may occur in any part of the tube

A complaint of persistent dysphagia by a patient who has pulmonary tuberculosis suggests the possibility of tuberculosis of the esophagus However, tuberculosis of the hypopharynx or larynx is commoner and usually will be found to account for the esophageal symptoms

In the absence of other nontuberculous lesions such as cardiospasm, diverticulum, or cancer, and in the presence of a defect in the esophageal shadow in a roentgenogram suggestive of ulceration or narrowing of the esophagus, the diagnosis is usually certain The endoscopic appearance of the lesion may arouse the suspicion that tuberculosis is present, but a positive diagnosis cannot be made without biopsy of tissue and guinea pig inoculation

The primary tuberculous disease is usually far advanced when the symptoms of esophagitis occur, and the prognosis therefore is grave.

Syphilis of the Esophagus. Tertiary syphilis of the esophagus may be responsible for a chronic esophagitis A syphilitic ulcer of the esophagus may result from the occlusion to a sizable nutrient vessel caused by syphilitic periarteritis A widespread syphilitic submucosal fibrosis of the esophagus gives rise to extensive narrowing of the lumen When present, gummas are often situated in the lower part of the esophagus or may be situated in the diaphragm at the hiatus oesophageus and may produce obstruction.

Syphilitic esophageal lesions may cause fibrotic stenosis and subsequently spontaneous rupture of the esophagus.

An esophageal lesion occurring in a patient who has untreated syphilis is regarded as possibly syphilitic and so treated if carcinoma can be excluded by endoscopic methods of examination and biopsy studies

Fungous Infections of the Esophagus. A
cause esophagobronchial fistula The diagnosis c
agus depends on microscopic examination of ma
agoscope and positive cultures of this material
pathogenic potentials to cause disease.

Fungous lesions of the esophagus are rare eve
blastomycosis

Esophageal Fistulas. Carcinoma, peptic ul
and actinomycosis, as well as foreign body and
esophagus In the middle-aged patient the mos
fistula is an ulcerating carcinoma. Fistula from
municates with the trachea or a large bronchus
sages rarely perforate into the esophagus

Respiratory symptoms, such as cough ass
blood, mucus and food, dyspnea superimposed o
and dysphagia are characteristic In addition
primary disease In a patient who gives an ante
currence of strangulation after swallowing sugge

Often the fistula can be discovered by roent
aperture is not seen by the endoscopist

If the fistula is large and the strangulation
or peroral gastric intubation will be required (
may be tried Some patients who have bronch
years

Esophageal Diseases Due to Trauma or P
of the esophagus sustained in accidents and p
discovered at necropsy

The presence of a foreign body in the esoph
tures can be diagnosed

Foreign Bodies. The stoppage of a foreign
a foreign body in the esophagus of an adult is
unsuspected, previously asymptomatic esophage
may be either a benign or a malignant steno
Therefore, after the removal of a food bolus o
agus, roentgenologic and often endoscopic exa

Foreign bodies such as fish bones may pu
pain and dysphagia Occasionally such an obje
mation of serious prognostic import

The diagnosis is evident from the history
vided the latter is performed by skilled hands

Rupture. The commonest cause of rupture
An esophageal rupture from instrumentation i
esophagus such as an esophagitis due to infecti

Rupture of the esophagus is followed by
choking sensation, retching, collapse, and ofte
ruptured from any other cause, the diagnosis is
examination

Esophageal Varices. The average age of the patient who has esophageal varices corresponds to the age incidence of portal cirrhosis (50 years), except in Banti's syndrome, which occurs at an earlier age.

When there is portal hypertension, an effort is made to establish collateral circulation, and the esophageal veins, because of the connection with the coronary vein and vasa brevia of the cardia, dilate and protrude into the lumen of the esophagus

Esophageal varices are symptomless When symptoms occur, they are referable to a single hemorrhage or to repeated hemorrhages as the result of rupture of a vein. There are often the accompanying symptoms of cirrhosis of the liver. The hemorrhage may be profuse and attended by death

Diagnosis of esophageal varices is made by roentgenoscopic examination The diagnosis may be suspected when hemorrhage occurs in a patient who has cirrhosis of the liver There may be value in performing both endoscopic and roentgenoscopic examination in order to determine the extent of the lesion

Hemangioma of the Esophagus. In a person who has dermal evidence or other manifestations of hemangiomas, there may be mild or profuse esophageal bleeding from one of these tumors These patients may be younger than those who bleed from esophageal varices or from portal hypertension, or they may be of the same age group as those who have Banti's disease Diagnosis is established by endoscopic examination

Deficiency Diseases of the Esophagus. *Plummer-Vinson Syndrome.* There is much to indicate that this syndrome is a type of iron deficiency anemia associated with a vitamin B complex deficiency Despite the plausibility of the theory of vitamin deficiency state, it has not been disproved that this syndrome is initially a hypochromic, microcytic anemia, an iron deficiency. The dysphagia in either case is best explained as the result of a pharyngo-esophagitis The psychic manifestations are concomitant or secondary, not primary.

A woman at the time of menopause who has a history of menstrual irregularity and a complaint of dysphagia accompanied by pallor, glossitis, pharyngitis, cutaneous changes, and enlarged spleen has a Plummer-Vinson syndrome, a vitamin B deficiency disease

The diagnosis of Plummer-Vinson syndrome is based on dysphagia, a microcytic hypochromic anemia and roentgenologic study which does not reveal an organic disease in the esophagus. Usually achlorhydria is present

Diseases of the Esophagus Due to Disturbances of Innervation. In most instances paralysis of the esophagus is situated in the pharynx and the upper part of the esophagus The paralysis may occur as a result of lesions of the vagus nerve, toxic neuritis or diphtheria A bulbar type of paralysis of the esophagus may be a complication of syringomyelia or the result of an atherosclerosis or any other bulbar lesions which give rise to dysphagia

Cardiospasm. Cardiospasm is known also as simple ectasia, atony and idiopathic dilatation of the esophagus, mega-esophagus, hiatal esophagism, functional hiatal stenosis, phrenospasm, preventriculosis and achalasia of the cardia

CAUSES. The following theories of cardiospasm have had their protagonists. (1) failure of relaxation of the cardia, (2) nutritional deficiency states, (3) psychogenic factors and (4) autonomic and other factors (Bockus)

1. Failure of Relaxation of the Cardia. In cardiospasm there may be failure of the [illegible] wave of contraction which is carrying [illegible] ophagus is not strong enough to over[illegible] ncter There are no objective data to support this contention.

2. Nutritional Deficiency States. Nutritional deficiency states have been held indirectly responsible in the etiology of some cases of cardiospasm There are only subjective data to support this contention.

3. Psychogenic Factors Often the onset of dysphagia follows nervous shock or grief, or emotional disturbances

4 Autonomic and Other Factors. A common cause of dysphagia is the too rapid swallowing of food or drink.

Peptic ulcer of the esophagus, esophagitis, and diverticulum in the lower part of the esophagus are in some instances responsible for the development of cardiospasm Toxic conditions caused by lead, alcohol, or the excessive use of tobacco may be accountable for the neuromuscular disturbances in some patients

SYMPTOMS. The symptoms commence with pain or discomfort, a sensation of pressure or burning or of food sticking temporarily at or near the lower end of the sternum In the beginning the symptoms may occur infrequently. Later the dysphagia recurs with increasing frequency and severity until eventually a sensation of fullness or discomfort behind the sternum may be almost continuous. The discomforts may be referred to the neck, lower jaw or region of the ears.

Pain resembling that of angina pectoris in distribution may be initiated by esophageal spasm The pain of cardiospasm is not provoked by exertion

Dysphagia may attend the ingestion of food or drink, an emotional upset, an acute infection or may appear during the night when the patient is recumbent, thus permitting some of the retained esophageal contents to pass into the trachea and respiratory passages, causing violent cough and choking.

Anemia, nutritional deficiencies and loss of body weight are commonly observed in those who have great and prolonged esophageal dilatation

A smooth constriction about an inch above the cardia, with or without dilatation of the esophagus, revealed on the roentgenogram justifies a provisional diagnosis of cardiospasm A history of dysphagia of years' duration indicates a benign stenosis. In some a period of observation, with several endoscopic and roentgenologic examinations, is required before a certain diagnosis of a benign lesion can be established.

A recurrence of symptoms may be anticipated following dilatation An occasional patient who has a cardiospasm will succumb to the effects of the disorder or of an accident during stretching of the esophagus

Diseases of the Esophagus Due to Unknown or Uncertain Cause. Single ulcers of the esophagus occur which are not peptic ulcers. These ulcers include lesions caused by the ingestion of caustics, by trauma, acute infectious diseases, traction diverticula, varicosities and those of indeterminate origin

Peptic Ulcer of the Esophagus. Esophageal peptic ulcers occur in the distal 3 inches (7.6 cm.) of the esophagus, frequently within 1½ inches (about 3 8 cm) of the cardia, and occasionally with extension into the cardiac end of the stomach. Often there is an accompanying peptic ulcer of either the stomach or the duodenum or of both.

Peptic ulcers may occur when there is a short esophagus or a diaphragmatic hernia They may result from regurgitation of acid gastric juice through a poorly functioning cardia, thus causing erosion and ulceration. Extensive surface burns may cause transient esophageal ulcers comparable to Curling's ulcer of the duodenum.

Peptic ulcer of the esophagus is often asymptomatic. When symptoms are present, they consist of pain and often dysphagia The pain, situated under the lower part of the sternum and often referred first to the back and then to the anterior part of the thoracic region, is the significant symptom It follows immediately after deglutition Pain which appears later after meals is due to an associated duodenal or gastric ulcer. Dysphagia may precede the occurrence of pain, may occur alone, or may be associated with regurgitation of food or drink

There may be anemia and loss of body weight and strength as the result of chronic bleeding Perforation may occur, which is usually fatal

Peptic ulcer of the esophagus is diagnosed by means of roentgenologic and endoscopic examinations

Tumors of the Esophagus. *Benign Tumors.* Benign tumors in the esophagus are rare. Perhaps these tumors occur at an earlier age than carcinomas. The sexes are equally affected

The commonest varieties of benign tumor are polyps, lipomas, myomas and fibromas. Other benign tumors less frequently encountered are papillomas, angiomas, hematomas, lymphangiomas and aberrant thyroid cysts The polyp is the commonest benign tumor in the esophagus.

Cysts occurring in the esophagus may be parasitic, dermoid, congenital, or retention cysts of the esophageal glands. At or near the bifurcation of the trachea is a common location for cysts These cysts may be the result of an imperfect separation of the embryologic connection between the esophagus and trachea.

Benign tumors cause symptoms like carcinoma of the esophagus except in patients younger than the patient who has esophageal carcinoma. Bleeding and dysphagia frequently occur from a benign tumor. Harrington reported an instance in which a long pedunculated polyp was ejected into the pharynx during the act of vomiting

The roentgenologic and the endoscopic examinations are essential for diagnosis The benign character of the tumor can never be established with certainty without histologic study

Malignant Tumors. Carcinoma of the esophagus generally occurs in the lower third of the viscus It is predominantly a disease of middle aged and aging men.

The two common histologic types of esophageal cancer are the squamous cell epithelioma and the adenocarcinoma The growth may project as a polypoid neoplasm into the esophagus or may encircle the esophagus and constrict its lumen In either case obstruction is a constant manifestation In some the tumor ulcerates and causes anemia, bleeding and early metastasis, and in these obstruction is late or absent

Carcinoma of the distal part of the esophagus often metastasizes to the liver, the cardiac end of the stomach, the inferior mediastinum, the lungs and occasionally to the vertebrae Carcinoma of the upper thoracic segment of the esophagus may spread to the trachea, and carcinoma of the upper third may invade the larynx, the pharynx, the thyroid or the recurrent laryngeal nerve

The symptoms commence with a sensation of food sticking and stopping on its way down The sensation is attended by substernal or neck pain After this symptom is established, there ensues a definite dysphagia The progress of the dysphagia is evident by the gradual elimination of solid food from the diet. In a few the first symptom appears after a foreign body has lodged in a narrowed, constricted esophagus and has been dislodged. More commonly the patient has had what is described as an inability to get the food down Then regurgitation or vomiting ensues Hoarseness is an uncommon complaint It is due to paralysis of the recurrent laryngeal nerve or is the result of direct extension of carcinoma into the larynx

A fistulous communication between the esophagus and the respiratory passages should be suspected from the onset of dyspnea and cough with the expectoration of blood, mucus and food Pulmonary abscesses, empyema and paralysis of a vocal cord rapidly ensue

The physical examination rarely reveals more than evidence of loss of weight and pallor The degree of emaciation may be extreme Occasionally lymph nodes may be palpated in the left supraclavicular, cervical, or axillary regions. The liver may be enlarged Frequently the swallowing sound on auscultation is delayed or absent

The diagnosis of carcinoma of the esophagus is based on endoscopic and roentgenoscopic examinations plus histologic examination of tissue removed for biopsy Negative results of biopsy, however, do not exclude absolutely the diagnosis of a malignant lesion It may be necessary to perform biopsy two or more times in a case of suspected carcinoma before malignant tissue is found Compression of the esophagus from an extrinsic lesion may cause great difficulty in diagnosis.

The average duration of life after the diagnosis has been established is approximately six months.

Sarcoma About 1 in 150 malignant lesions of the esophagus will prove to be a sarcoma. The symptoms are the same as those of carcinoma of the esophagus The findings on roentgenologic and esophagoscopic examinations do not distinguish sarcoma from carcinoma The differential diagnosis is made by a histologic study of tissue removed through the esophagoscope.

THE ABDOMEN

(Exclusive of the Pancreas, Spleen and Genitourinary Tract)

The abdomen comprises the section of the body that is anterior, in the center, to the lower portion of the thoracic, lumbar, sacral and coccygeal regions of the spinal column, and on the sides to the erector spinae and quadratus lumborum muscles. In front it extends from the diaphragm above to the rim of the pelvis below.

The shape of the abdomen is influenced by its bony support, by the tone of its muscles and the strength of its fascia, and by the size of the organs and the amount

ensiform

vertebra

ium—the

sixth and seventh costal cartilages meet at this point—also can be felt The seventh, eighth, ninth and tenth costal cartilages can be followed down to the lower border of the thorax The eleventh rib, which is free, can be distinguished The twelfth rib is often not palpable

The spines of the pubes as well as the upper edge of the pubic bones can be identified The depressions for the fasciae of the linea alba, lineae semilunares and lineae transversae are all more definite above the umbilicus than below it

REGIONS The abdomen arbitrarily is divided into regions so that the location of particular portions can be specified In precise descriptions the surface views are divided into 9 regions by 2 transverse and 2 longitudinal lines (Fig 13-1) The upper transverse line passes from the tip of the tenth rib, which corresponds to the lower end of the thorax, on one side to that of the other The lower transverse line passes from the anterior superior spine of the ilium on one side to that of the opposite, it is on a level with the second sacral vertebra. The two longitudinal lines pass directly up on each side from the middle of Poupart's ligament

The middle regions are the epigastric, the umbilical, and the hypogastric or pubic The lateral regions are the right and left hypochondriac, the right and left lumbar, and the right and left iliac

It is more convenient for descriptive purposes to divide the abdomen into four quadrants by a longitudinal median line and a transverse line through the umbilicus (Fig 13-2) Both of these divisions of the abdomen into regions are used and their usage depends on the applicability

LINES OR LINEAE There are certain lines on the abdomen, called linea alba, lineae semilunares, and lineae transversae, and sometimes there are present lineae albicantes

The *linea alba* passes in the median line from the ensiform cartilage to the symphysis pubis. It is formed by the fusion of the sheaths of the recti muscles A failure of fusion of these sheaths or a separation of them during the course of pregnancy or of the growth of large abdominal tumors may permit sufficient separation so that impulses originating in the abdomen can be felt

Between the transverse fibers of the sheaths of the recti muscles there may be gaps These gaps may be large enough to allow the subperitoneal fat to protrude and form a hernia in the median line which can be felt under the skin as a small, firm, rounded body

The *lineae semilunares* are not readily recognized by palpation.

On contraction of the rectus muscle in thin muscular persons grooves are seen on

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The innervation of the front and sides of the abdomen is supplied by the anterior and lateral cutaneous branches of the sixth, seventh, eighth, ninth, tenth and eleventh intercostal nerves, the twelfth thoracic and the iliohypogastric and ilio-inguinal branches of the first lumbar The sides of the abdomen are supplied by muscle branches

Besides the muscular innervation of the abdominal wall there is a connection of the cutaneous supply with that of the abdominal organs The areas of cutaneous hyperalgesia occurring in visceral disease are identical with the areas which receive their sensory nerve fibers from the spinal segment to which the afferent sympathetic fibers from the diseased viscera pass Head demonstrated that the sixth, seventh, eighth and ninth thoracic segments receive afferent fibers from the stomach, the ninth, tenth, eleventh and twelfth thoracic segments, from the intestinal tract, the seventh, eighth, ninth and tenth thoracic segments, from the liver and gallbladder, the tenth, eleventh and twelfth thoracic, and the first lumbar segment, from the kidneys and ureters; and the second, third and fourth lumbar segments from the rectum These areas of hyperalgesia occur, but to attempt to determine their presence subjects an ill patient to too great an ordeal to justify the meager diagnostic data obtained.

The Hernias. A hernia is a projection of a viscus or part through a natural or accidental opening in the wall of the cavity normally containing the viscus The term is qualified by the name of (1) the protruding part, (2) the cavity from which it escapes, (3) the structure or part through which it passes, and finally, sometimes, (4) the cavity which receives it A hernia therefore is a projection of a viscus from the cavity in which it naturally is contained, the lining membrane of the cavity being projected before it. This lining membrane will be referred to hereafter as the hernial sac or the sac

The abdominal cavity is completely surrounded by muscles. The bony support is posterior and caudal The contents of such a cavity are prone to herniation

VARIETIES When the projection is outward, beneath the skin or toward it, the hernia is external (subcutaneous, intermuscular or properitoneal), when within the body, in one of the larger body cavities, it is internal

The external hernias include (1) inguinal hernia, direct or indirect, (2) crural, or femoral, hernia, below Poupart's ligament, (3) umbilical hernia, (4) abdominal hernia, especially in the linea alba.

The internal hernias include (1) diaphragmatic hernia, recognizable in roentgenograms, (2) retroperitoneal hernias, (A) in Treitz's fossa, (B) in the recesses intersigmoideus and (C) in the foramen epiploicum of Winslow

When a hernia cannot be returned, but is fixed by adhesions or otherwise, it is said to be irreducible The most important complication is incarceration (not synonymous with irreducibility), which may lead to ileus and to strangulation

In investigating a case of suspected hernia, make a systematic examination as follows: (1) Does a hernia actually exist? (2) Is the hernia incarcerated? (3) What does the hernial sac contain? (4) What is the exact site of the incarceration?

TRAUMA AS A CAUSE OF HERNIAS. The physician is often asked for an opinion in regard to the effects of trauma as a causative agent of hernia

Acute traumatic hernia is rare Usually the condition develops gradually, owing to repeated strain beyond endurance of the weakened or abnormally patent inguinal rings or other natural or artificial openings due to congenital weakness of these structures or to weakness following surgical operation or injury The hernia in its incipient stage may exist for many months previous to being observed by the patient It can hardly be conceived that a hernia, inguinal or otherwise, can entirely and suddenly be brought about by severe strain unless there is a pre-existing formation of the mechanical changes such as the sac that produces the bulging It is possible, however, for such a pre-existing formation to become injured and as the result of such injury the individual's attention is for the first time called to abnormality of the region

However, in practice, in a particular instance of inguinal hernia, the hernia may

These tendinous intersections are the remains of the intersegmental septa which separate the original myotomes One is just above the umbilicus, a second *opposite the tip of* the ensiform cartilage, a third midway between these two, and sometimes there is a fourth below the umbilicus.

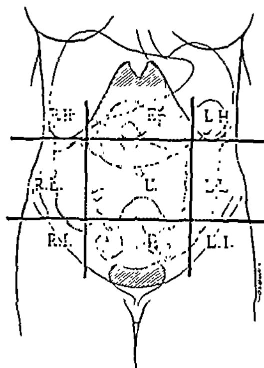


Fig 13-1 Topographic regions of the abdomen for precise description R H, right hypochondrium; R.L, right lumbar, R I, right inguinal, Ep, epigastrium, U, umbilical, P, pubic; L H, left hypochondrium, L.L, left lumbar, L I, left inguinal

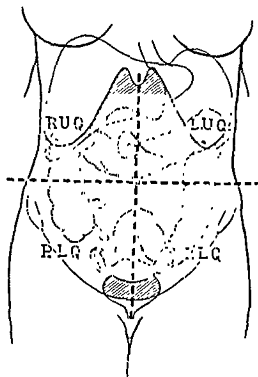


Fig. 13-2. Quadrants of the abdomen R U Q, right upper quadrant, R.L Q, right lower quadrant, L U.Q, left upper quadrant; L.L Q, left lower quadrant

Lineae albicantes are the faint, white, atrophic lines left in the skin of the abdomen after it has been hyperdistended, usually by pregnancy or tumors

The groove formed by Poupart's ligament runs from the anterior superior spine of the ilium to the spine of the pubis

The Abdominal Walls. The abdominal walls are composed of the skin, muscles and associated superficial and transversalis fasciae, blood vessels, lymphatics, and nerves.

The *skin* of the abdomen is moderately thin and lax It is adherent at the linea alba

The *muscles* of the abdomen are arranged in two distinct groups· a longitudinal group embracing the *recti* and *pyramidales* and a transverse group embracing the *external* and *internal oblique* and the *transversalis* of each side The abdominal muscles are rarely paralyzed.

The upper part of the abdomen is drained by small superficial veins which empty into the superior epigastric, the intercostal, and laterally into the axillary veins All the other abdominal veins drain into the inferior vena cava. When small veins around the umbilicus become enlarged and branch in various directions, the condition is termed *caput medusae*.

The superficial parts above the umbilicus are drained by *lymph vessels* which empty into the axillary nodes, the vessels below the umbilicus empty into the oblique set of nodes in the groin. The lymphatic channels of the deep surface of the abdominal wall above the umbilicus drain into the mediastinal nodes, while those below drain into the pelvic lymphatics along the iliac arteries

Inguinal hernia occasionally occurs in the female. There it presents itself at the inguinal canal or may follow the round ligament of the uterus into the labium majus pudendi The round ligament is homologous to the gubernaculum testis in the male.

There are two kinds of inguinal hernia, the *congenital* and the *acquired* and each of these may be indirect or direct. *Indirect* inguinal hernias are usually congenital, the degree being only a variation in the quantitative expression of a congenital defect existent at birth

The *direct* inguinal hernias may be the result of a developmental defect of the internal oblique and the transversalis muscles or more usually of the conjoined tendon, or they may be an acquired condition, the result of asthenia and debility

A direct inguinal hernia presents directly through the abdominal wall and not through the inguinal canal The hernia appears in the neighborhood of the external ring or may cause a protrusion of the abdominal wall just above and to the inner side of the ring

SYMPTOMS An inguinal hernia is observed by the patient as a protrusion or a mass in the groin It is accompanied by a moderate amount of pain during the first few days It may or may not be preceded by a history of undue strain The pain decreases, so that in a week or two the symptoms consist of nothing more than a feeling of discomfort

Frequently the history is given of the patient's having been examined by an industrial physician who found a dilated external ring and a transmitted impulse on

found if diligently sought for by the surgeon

EXAMINATION A precise method of physical examination for detection of the presence of hernias of the inguinal and the femoral regions has been outlined by Zieman

The patient is examined in the upright position with the examiner standing somewhat behind and to the right, using the right hand for a right inguinal hernia, and to the left, using the left hand for a left inguinal hernia This method in no way distorts the relationships of the parts in this region and it obviates a palpation artefact The examining hand is so placed that the first, second and third fingers lie over the inguinal region in such a manner that the index finger rests about 2 or 3 cm. above the inguinal canal. The middle finger lies along the direction of the inguinal canal with the tip of the finger at the external inguinal ring, while the third finger controls the femoral canal and the fossa ovalis With the hand in this position it is possible to perceive a distinct sliding, pushing motion of a viscus under one or another of the examining fingers when the patient is directed to cough or strain Thus a direct or an indirect inguinal hernia or a femoral hernia may become apparent If there is a bulging mass apparent to the eye, the examining hand forces the mass inward, and again coughing or straining immediately differentiates the type of hernia present The palpation of a bubbling mass which slides back into the abdomen determines the presence of a hernia

The usual method of examination for inguinal hernia is to pass the index finger along the spermatic card until the external inguinal canal is identified A bulging through the canal through which the impulse of a cough is transmitted indicates an inguinal hernia

DIAGNOSIS An inguinal hernia can hardly be confused with any other condition in these regions Enlargement of the inguinal or the femoral lymph nodes may resemble a hernia of the irreducible type. A lipoma over or in the inguinal canal presents a similar resemblance Acute inguinal lymphadenitis will usually be associated with pain and other inflammatory signs which, however, may also be demonstrable over a strangulated hernia The sudden development of symptoms accompanying strangulated hernia is usually sufficient to establish a correct diagnosis. Occasionally

be alleged to be of traumatic origin The patient relates a history of sudden pain in the groin associated with the appearance of a hernial mass immediately following a strain such as lifting. It should be stated that compensation boards usually consider trauma as being capable of producing hernias

Swelling from other causes may occur in the inguinal region and claim may be made of trauma as the cause. Gonorrheal and chancroidal bubo, epididymitis, and other infections and tumors may cause enlargement of lymph nodes in this region

Inguinal Hernias, Congenital and Acquired, Direct and Indirect. The *inguinal canal* (*canalis inguinalis*) runs from the external to the internal abdominal ring and is about 1¾ inches (4 5 cm) in length. The external ring barely admits the tip of the finger; it lies immediately to the outside and above the spine of the pubis. It is formed by a splitting of the fibers of the external oblique aponeurosis into two columns or pillars. The *internal column* (*crus superius*) inserts into the crest and anterior surface of the body of the pubis The fibers running across from one column to the other are the intercolumnar fibers (fibrae intercrurales) and are prolonged over the cord as the intercolumnar fascia

The internal ring (annulus inguinalis abdominalis) is the opening in the transversalis fascia where the spermatic cord in men and the round ligament of the uterus in women enters the canal

The body being upright, the inguinal canal has an anterior and a posterior wall, a roof and a floor It is ½ to ¾ inch (1.2 to 4.5 cm) long The anterior wall (nearest to the skin) is formed by the aponeurosis of the external oblique muscle and by the internal oblique muscle for its outer half The posterior wall is formed by the transversalis fascia and, at its inner third, the conjoined tendon The roof, toward the abdominal cavity, is formed by the arching fibers of the internal oblique muscle and, still farther above, the transversalis The *spermatic cord or round ligament* in the canal rests on Poupart's ligament

The foregoing anatomic structures were occasioned by the origin and descent of the *testicles* The testicle originates, about the third month of fetal life, in the lumbar region inside of the abdomen It is behind the peritoneum and has a fold of peritoneum, the plica vascularis, passing upward from it, containing the spermatic artery and veins, and a fold called the gubernaculum, passing downward to the inguinal region and into the scrotum. By the fifth or sixth month of fetal life the testicle has reached the abdominal wall at the internal ring, after which it enters the inguinal canal to pass into the scrotum *in the eighth or ninth month of fetal life. A process of peritoneum, the vaginal process,* precedes the passage of the testicle into the scrotum The neck of the vaginal process is called the funicular process Soon after birth the vaginal process becomes occluded, first at the internal ring, and thence downward until the testicle is reached, where the unobliterated portion forms the tunica vaginalis

During the descent of the testicles and the disposition of tissues which ensues, certain anatomic developmental defects may occur The resulting hernias are termed in accordance with their relationship to these defects vaginal (congenital), funicular, encysted, and infantile

In *vaginal hernia* the vaginal process remains entirely open and the intestine passes down into the scrotum The testicle is found protruding into and at the bottom of the hernial sac. In *funicular hernia* the vaginal process is occluded just above the testicle, but the funicular process remains open and the intestine descends into it If the vaginal process is occluded at the internal ring only, the remainder forms a continuous sac below containing the testicle. In *encysted hernia* the intestine descends and pushes the vaginal process before it down into the cavity containing the testicle. In *infantile hernia* also the vaginal process is occluded but only at the internal ring As the intestine descends, it forms a sac posterior to the point of occlusion and vaginal process

The *interparietal* (*interstitial*) *hernia* is a variety of oblique hernia It is often associated with anomalies of the testis It is so called because it does not emerge through the external ring, but presents itself through the layers of the abdominal wall.

the factor which prompted surgical intervention In every case reviewed, operation was performed

Intra-abdominal Hernias Referable to Congenital Malformations. Instances of congenital malformation of the primary midgut loop, excluding the duodenal hernia, have their origin in malrotations or improper fusion of the peritoneal layers, either of the mesentery of the small intestine, or of the cecum and the ascending part of the colon Persistent traction bands may also be found in such cases Defective disposition of the small intestines and right part of the colon, a process commonly termed malrotation, may account for hernias

Improper fusion of the peritoneal layers of the postarterial segment will result in the formation of small pouches under the cecum and ascending part of the colon. Retrocecal hernias are often found during the performance of surgical procedures for other conditions.

An internal hernia involving the mesentery of the small intestine may be present when prolapse of the bowel through an aperture lying between the ileocolic artery and its last mesenteric branch has taken place

The occurrence of internal herniation through the foramen of Winslow is extremely infrequent, because of the barrier afforded by the transverse part of the colon According to Mayo and Miller, one of the following factors must be present to permit the formation of this particular type of hernia: (1) A common mesentery for the whole intestine, (2) absence of secondary fusion of the ascending part of the colon to the abdominal wall, (3) an abnormally large foramen; and (4) an abnormal length of the mesentery and consequent marked mobility of the intestine In some instances a Meckel's diverticulum may remain attached to the abdominal wall, producing a bandlike structure These bands and adhesions are occasionally the cause of herniation, with resulting intestinal obstruction. Herniation into the prevesical space or the space of Retzius is rare

Postoperative Intra-abdominal Hernia. Intra-abdominal hernia, as a postoperative complication, may be immediate or delayed Failure of the transverse mesocolon to remain attached to the stomach following posterior gastroenterostomy may result in an aperture through which a loop of small intestine may slip into the lesser peritoneal sac and cause obstruction Hernias have been reported to afflict patients subsequent to resection of the stomach with anastomosis to the jejunum The presence of this type of hernia is difficult to recognize but in those cases in which gastrojejunostomy has been performed and symptoms of intestinal obstruction develop, or in which some mechanical defect in the anastomosis is present, the possibility of herniation must be considered Adhesive bands resulting from inflammation can form the opening through which the bowel may herniate These occur more commonly after various pelvic operations and secondary to operations for ruptured appendix

Subsequent to an operation for retroversion, some error in technic may occasionally be the cause of formation of an internal hernia In other instances, in performance of such operations as myomectomy, oophorectomy, appendectomy, and the like, openings are inadvertently made in the broad ligaments In the performance of other pelvic operations in which the uterus is suspended, instances of herniation of intestine between the uterus and the anterior abdominal wall have been recorded

Various apertures may occur in the omentum as a result of trauma or infection following operation

Paraduodenal Hernia. Many fossae about the duodenum have been minutely described, but proof that they are a factor in the causation of hernias with clinical manifestations is lacking

Left duodenal h[illegible]

[illegible] ıe contra-
[illegible] re usually
[illegible] explored

a psoas abscess may present in the inguinal region and produce a bulging mass which resembles a hernia.

Postoperative (Incisional, Ventral) Hernia. Suppuration of a wound in the abdominal wall is conducive to formation of hernia. Although hernia is likely to follow operation for drainage of intra-abdominal abscesses, for example, appendical abscess, only a few postoperative hernias are due to suppuration. Postoperative hernias occur most frequently in fat persons. Any pulmonary complication which results in frequent coughing during the first 5 or 6 postoperative days may produce a hernia, or even produce a rupture of the wound.

If the fatty subcutaneous tissue is thick, the hernial mass may burrow for a considerable distance subcutaneously The hernial opening often enlarges so that a large proportion of the contents of the abdominal cavity is eventually contained in the sac. The omentum becomes adherent to the sac, and if the sac becomes adherent to loops of intestine also, as it frequently does, the greater portion of the hernia may become irreducible

When the hernia first develops, the patient nearly always complains of a dragging pain arising in the neighborhood of the scar, but perhaps extending deep into the abdomen

Early in the formation of the hernia, tenderness at the site of the defect is pronounced When the hernia develops within a few days after laparotomy, because of partial rupture of the deep layers of the wound, the intestines herniating into the defect may at times become adherent and obstructed Usually, however, definite evidence of a hernia is not demonstrable, subjectively or objectively, for several weeks or months after operation

In some patients there is a general weakness of the abdominal wall which has developed postoperatively Such a weakness may permit of local bulging of the abdominal contents without actual herniation

The history, the reducibility, the impulse on palpation and particularly on coughing are unmistakable.

Intra-abdominal Hernia. Hernias that protrude into an abdominal pouch or opening of the peritoneum may be considered to be intra-abdominal or internal hernias These may be primary, a direct result of some congenital defect; secondary or postoperative sequelae, or referable to trauma or inflammation not the result of an operation. Thus, they include (1) those which occur in normal pockets, such as the foramen of Winslow, paraduodenal, paracecal, and intersigmoidal fossae; (2) those occurring in exaggerations of normal mesenteric folds, such as those in the broad ligament; (3) those resulting from traumatic or operative bands or adhesions; (4) those resulting from chronic inflammation, and (5) those which occur in anatomic defects.

A classification of internal hernias is difficult Intra-abdominal hernias have been classified by Mayo, Stalker and Miller into four groups. (1) congenital malformations, (2) postoperative, (3) paraduodenal and (4) miscellaneous

In the 39 cases reported by Mayo, Stalker and Miller, 21 (54 per cent) were considered to be secondary, and 18 (46 per cent) primary. In 20 instances the hernia developed secondarily, previous to performance of some surgical procedure

The symptoms presented by the hernias were, for the most part, varying degrees of intestinal obstruction In 29 cases (74 per cent) the hernia was considered to be producing symptoms, and in 10 cases (26 per cent) no symptoms were caused In the 10 cases in this latter group the hernia was observed incidentally at the time of operation for some other condition The symptoms, for the most part, were vague and not characteristic A preoperative diagnosis seldom was made Some degree of obstruction of the small intestine was present in 28 (72 per cent) of the cases. In 19 cases (49 per cent) the onset was marked with acute obstruction of the small intestine. When obstruction was not present, pain or the presence of a tumor was

syphilis of the umbilicus at or shortly after birth and (3) syphilis of the umbilicus in the adult.

The diagnosis is established by darkfield and serologic examinations and association with a proper history

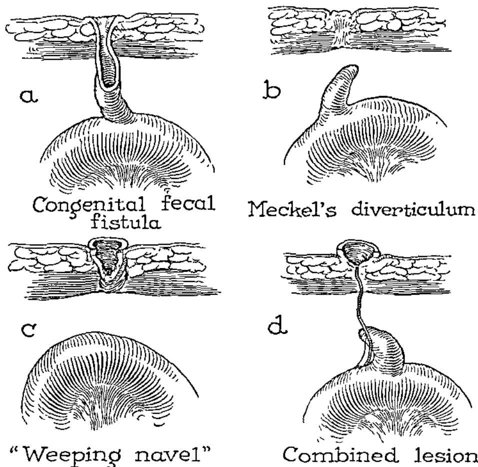


Fig 13-3 Schematic representation of varying degrees of persistent omphalomesenteric duct a, patent duct b, umbilical end obliterated with Meckel's diverticulum remaining c, the intestinal end obliterated but active mucous membrane situated in the umbilicus d, Meckel's diverticulum, persistent cord and mucous membrane in navel

Fecal Fistulas at the Umbilicus. Umbilical fistulas may be due to a patent omphalomesenteric duct, to inflammatory changes commencing in the intestine and extending to the umbilicus, to carcinoma of an abdominal organ, usually of the stomach, reaching to and breaking through the umbilicus, to inflammatory conditions of the umbilicus extending to and involving the intestine, and to external injuries

Umbilical Concretions Associated With Inflammatory Changes in the Abdominal Wall. In those who have umbilical concretions the umbilical opening

The pain may be increased on muscular exertion, on defecation, or on pressure upon the abdomen.

On visual examination sometimes nothing is detected Later, induration is noted

for other reasons. However, occasionally when obstruction, acute or chronic, or strangulation supervenes, the patients have symptoms

Miscellaneous Intra-abdominal Hernias. There are intra-abdominal hernias which cannot be satisfactorily classified Occasionally, *secondarily to some inflammatory* condition such as pelvic inflammatory disease or appendicitis *for which* surgical intervention was not performed, adhesive bands may form between which herniation or strangulation of the intestine may occur.

There are often present mesenteric and omental defects for which a cause cannot be assigned In the absence of a suggestive cause, many are thought to be of congenital origin. Rupture of the omentum or the mesentery as a result of external violence, or of injury during the course of a previous surgical operation, is considered to be possible cause in some instances In some cases, antecedent inflammation of the appendix with involvement and subsequent atrophy of mesentery or omentum may produce such a defect In the absence of both trauma and a previous operation these defects of the mesentery and omentum with subsequent hernia formation must be considered to be secondary to some congenital fault

Internal hernias become manifest through various degrees of intestinal obstruction, though some internal hernias are manifested by pain and formation of tumor.

The diagnosis of intra-abdominal hernia is seldom made prior to operation or postmortem examination.

Strangulated Hernia. *Strangulation does not develop until several hours after* the hernia becomes obstructed When strangulation develops, tension within the mass increases There is an increasing difficulty in reduction and soon reduction may become impossible Nausea and vomiting ensue The pain increases and becomes persistent The pain at first is poorly localized, but soon becomes most prominent in the mass, extending frequently into the depth of the abdomen. Prostration and a fast small pulse develop rapidly There may be mild collapse, with a cold, pale and moist skin, especially if a large amount of intestine is involved in the strangulation. The manifestations of intestinal obstruction ensue

On rare occasions strangulation may occur in an internal hernia The strangulation of an internal hernia is not diagnosed prior to operation In an occasional instance of strangulation of an internal hernia in an elderly patient the symptoms are ill defined and of a minimal degree and the diagnosis in such cases may be made at *postmortem examination*

THE UMBILICUS

The umbilicus varies widely in its location It is always in the midline of the abdomen but its cephalocereal level depends on the tone of the abdominal musculature and the quantity of the abdominal contents The vitelline duct in fetal life passes from the umbilical vesicle to the small intestine Normally it entirely disappears If its proximal extremity persists, it forms a Meckel's diverticulum (Fig. 13-3). If its distal end persists up to the umbilicus, there is a fistula through which feces may discharge If the lumen is obliterated, a fibrous cord may persist which may cause strangulation of the intestine The stalk of the allantois ends as the urachus, running down to the fundus of the bladder. If the urachus remains patulous, urine may be discharged through the umbilicus.

Infections of the Umbilicus. The umbilicus is singularly free of disease Low-grade umbilical infection and eczemas are common, however, and, ringworm, of the same species which *affects the intertriginous folds* of the body, occurs therein

Tuberculosis. Tuberculosis of the umbilicus is exceedingly rare It occurs when a tuberculous bowel becomes adherent to and opens through the umbilicus. The diagnosis is proved by guinea pig inoculations with biopsy or aspirated material from the umbilicus.

Syphilis. Syphilis of the navel is rare, but when it occurs, *it may be divided* into three groups for purposes of classification· (1) chancre of the u

contracts, a good deal of urine may be forced into the urachal pouch. In these cases the urine stagnates, decomposes, and constitutional symptoms ensue.

From time to time a tumor forms between the umbilicus and the pubes. This usually gives the patient considerable pain, and its presence is sometimes accompanied by fever.

The first manifestation usually is enlargement of the lower part of the abdomen in the midline, but the swelling, sometimes accompanied by pain, may first be observed in the right iliac fossa, and the symptoms may suggest appendicitis.

With the increase in abdominal girth, there may be a moderate degree of indigestion, and in some cases when the cyst has reached large proportions, dyspnea is present. Some of the patients become progressively emaciated and lose strength.

Micturition is normal in some, frequent in others The bladder may be encroached upon since the extent of the tumor is limited, on the one side by the peritoneum, and on the other by the anterior abdominal wall

Pain is a feature in some cases, absent in others The cyst is separated from the abdominal contents only by a thin peritoneum, and consequently the slightest inflammation of the cyst wall must extend to the peritoneum and produce pain and cause the omentum or some other abdominal structure to become adherent to the abdominal wall over the cyst

On physical examination an abdominal swelling is observed This may extend over the entire abdomen, or be limited to the lower portion. In some cases definite fluctuation can be elicited.

The diagnosis is usually obvious if the possibility of the condition is kept in mind Urachal cyst may resemble a distended bladder, ascites appendicitis with abscess formation, a cyst, localized peritonitis with a serous exudate under the anterior abdominal wall, and tuberculous peritonitis

Umbilical Hernias. Umbilical hernias are of three kinds, congenital, infantile and acquired

Congenital umbilical hernia is due to a developmental defect If development is interfered with, a cleft is left in the umbilical region into which intestine or other organs may protrude. If only intestine protrudes, it pushes up into the umbilical cord and constitutes a congenital umbilical hernia If the urachus remains patulous, it may form a urinary fistula The hypogastric arteries become obliterated and, opposite Poupart's ligament, have two fossae, one to their outside and one to their inside. Into these fossae direct inguinal hernias may pass The persistence of the vitelline duct may cause a finger-like projection, called Meckel's diverticulum, on the ileum, about 2 or 3 feet (61 0 or 91 4 cm) above the ileocecal valve Sometimes a band passes from Meckel's diverticulum to the umbilicus and causes strangulation of other coils of the intestine

Infantile umbilical hernia is the common form which appears soon after birth It does not contain omentum so constantly as does adult hernia, because it does not hang so low, nor is it so well developed

Acquired umbilical hernia is the form seen in adults The presence of the urachus and hypogastric arteries so strengthens the lower edge of the umbilical ring that hernial protrusions make their exit above, hence the hard edge of the ring is nearer the lower end of the umbilical hernial sac

The symptoms of umbilical hernia may appear either in infancy or in late adult life The first evidence of a hernia in childhood is evinced by a protrusion of the umbilicus when the child cries Such a hernia rarely produces any demonstrable symptoms Occasionally these hernias may enlarge until intestine also protrudes into the sac

Umbilical hernias in adults occur usually in the latter part of life and are three or four times more common in women than in men Relaxation of the abdominal muscles during pregnancy and obesity seems to be important. The skin over the hernia is thin and often bluish in color The subcutaneous tissue is often absent between the thin skin and the contents of the sac The symptoms of umbilical hernia

in the umbilical region, the umbilical opening becomes very small, and the surrounding tissue feels hard. The overlying skin may or may not be reddened. At this stage the patient may have excruciating abdominal pain, followed by the escape of a foreign body together with some blood and pus. A speedy disappearance of the symptoms usually follows.

Occasionally an umbilical concretion may be present without producing any inflammatory reaction

The Escape of Various Foreign Substances From the Umbilicus. Gallstones. The patients as a rule give the usual history of gallstones. Sometimes the initial pain is in the gallbladder region, but occasionally it is first noted in the left side of the hypochondrium, after a time it shifts to the right side In addition to the hepatic colic noted, there are sometimes nausea, vomiting, and diarrhea After a varying length of time, changes may be noted at the umbilicus. Abscess formation progresses rapidly, the stones are evacuated when the abscess is lanced or may be discharged spontaneously

Roundworms. The majority of the patients have symptoms of a gastrointestinal disturbance After a period varying from a few days to a couple of weeks soreness develops at the umbilicus, the center of the umbilicus gradually becomes softened, and the surrounding portions are thickened and edematous

In the course of a few days the abscess breaks and there is an escape of pus Sometimes this is accompanied by fecal matter or roundworms or both; occasionally fecal matter is not detected at all, the wound closing up after the pus and worms have escaped The worms may be alive or dead Occasionally only one worm escapes but, as a rule, several come away at once Closure of the wound may occur temporarily, only to be followed by more pain and the expulsion of more worms

The Urachus. Urachal remains occasionally communicate with the umbilicus or with the bladder or with both (Fig 13-4) There is usually a history of vesical

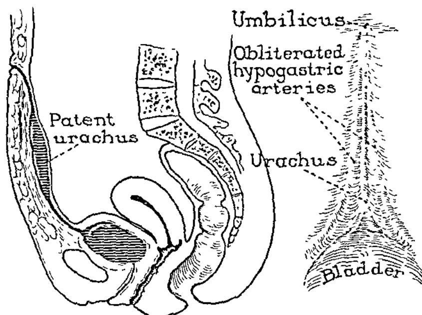


Fig. 13-4 Schematic representation of persistent urachus

irritability, and from time to time pus is passed with the urine. Sometimes the urachus is in reality an alcove from the bladder, the opening being very wide and assuring complete emptying of the cavity each time the bladder is evacuated On the other hand, if the communicating opening is very small, whenever the bladder

wounds in the abdomen and from the rupture of normal graafian follicles, and the peritonitis occurring in the course of septicemia and following surgical operation.

SYMPTOMS Acute peritonitis commences with generalized abdominal pain which is intense and is aggravated by movement and pressure The patient, if physically able, assumes a position which relieves the tension of the abdominal muscles. The usual position assumed is flat on the back, with the thighs drawn up and the shoulders elevated The patient desires to be left alone and is definitely annoyed by questions and examinations He is apprehensive and mentally preoccupied. The most intense pain usually is below the umbilicus except that in peritonitis from perforation of the stomach, duodenum or gallbladder the pain may be in the epigastrium and it is often referred to the back, thorax or shoulders

Respiration is superficial, costal and painful. Coughing is restrained In contrast to the foregoing symptoms an occasional patient may have an acute peritonitis, with a limited amount of pain, or the pain may be absent.

Vomiting is an early and prominent symptom and causes the patient a great deal of pain and discomfort As the disease progresses, the vomitus begins to be a brownish or black liquid When the sensorium is dulled by fever, there may be no symptoms indicating the onset of the peritonitis

EXAMINATION The abdomen is very tender and the muscles are rigid. The abdomen soon becomes distended and tense, and tympanitic, and respiratory movement in the abdomen is absent The pulse is rapid, small, hard and often has a quick rebound (pulsus celer). The pulse rate varies from 100 to 150. The rate usually increases as the disease progresses. After 24 to 48 hours the temperature may recede somewhat and remain at from 101 to 102 F (38 3 to 38 8 C) until near the end In acute peritonitis in an enfeebled patient there may be diminished pain and few systemic reactions, and there may be no fever

A group of signs designated as rebound phenomena includes rebound tenderness. Rebound tenderness is induced by sudden release of a pressure of the hand firmly applied to the abdomen The rebound phenomena also include pain induced on walking or by sudden flexion of one thigh, pain experienced on inward rotation of the leg, and pain produced on coughing

When the abdomen is auscultated, peristaltic noises are not present; an occasional tinkle of a bubble of gas in the intestine may be heard. The heart and the voice sounds are usually freely transmitted to the abdomen Vocal fremitus is often transmitted to all parts of the abdomen Usually the diaphragm is elevated and the hepatic dullness may disappear As the disease progresses, there may be effusion of fluid into the peritoneal cavity

A patient may have acute generalized peritonitis; in two hours the peritonitis may have begun to be localized, and thus the signs may change into those of localizing peritonitis If localization of acute peritonitis does not take place, the disease is rapid in its progress and usually is fatal

Acute secondary peritonitis always tends to *localize*, thus giving the symptoms of an abscess in the vicinity of its localization However, localized or circumscribed peritonitis may change into acute generalized peritonitis

The symptoms of localized peritonitis depend on the situation of the infected organ which is producing the peritonitis Since localizing peritonitis more often is produced by appendicitis or pelvic abscess than by other causes, it is most frequently situated in the right iliac fossa and in the pelvis

In women the commonest causes of pelvic peritonitis are puerperal septicemia, gonorrhea and tuberculosis of the internal genitalia In these conditions there are signs of a localized peritonitis or abscess in the pelvis.

DIAGNOSIS The diagnosis of a generalized, or a localized, primary or secondary acute peritonitis depends on obtaining the history and observing the afore-mentioned findings

in adults may not be pronounced The development of cramping pain, nausea and, especially, vomiting, indicates partial or complete intestinal obstruction. On account of the thin skin and the protrusion of the mass, the skin becomes traumatized readily and ulceration may develop. As the duration of the hernia increases, irreducibility becomes more pronounced Strangulation is uncommon

DIAGNOSIS The diagnosis is usually obvious. Lipoma of the umbilical region may have to be differentiated.

Tumors of the Umbilicus. Cullen listed both benign and malignant tumors of the umbilicus. There are both primary and secondary malignant tumors. The secondary malignant tumors which are secondary to intra-abdominal malignant disease are the commonest of all tumors of the umbilicus.

The benign tumors include (1) hypertrophy of the umbilicus; (2) angiomas; (3) lymphoceles; (4) benign connective tissue growths, (a) myxomas, (b) fibromas, (c) papillomas and (d) lipomas The ordinary umbilical papilloma is caused by a proliferation of the stroma, the squamous epithelium covering the papillae occupies merely a passive role It is for this reason that these small tumors are grouped with the benign connective tissue growths There are also (5) dermoid cysts; (6) sweat gland tumors; (7) abdominal myomas springing from the umbilicus, (8) papillomas secondary to growth in an ovary; and (9) adenomyomas

Malignant tumors of the umbilicus include carcinoma, primary and secondary, and sarcoma.

Primary carcinoma is of two types (1) squamous cell carcinoma and (2) adenocarcinoma. *Secondary carcinoma* arises (1) from the stomach, (2) from the gallbladder, (3) from the intestine, (4) from an ovary, (5) from the uterus and (6) from other abdominal organs

Sarcoma is classified as (1) telangiectatic myxosarcoma, (2) spindle cell sarcoma, (3) round cell sarcoma and (4) melanotic sarcoma.

THE PERITONEUM

Peritonitis. The peritoneum, pleura, and pericardium are derived from the celomic cavity The reactions of these structures to infections are analogous The entrance of an infecting agent into the pericardial, the pleural, or the peritoneal cavity is followed immediately by a heavy outpouring of exudates In all, there is a tendency to form fibrinous adhesions in an attempt to localize the infecting process

The peritoneal cavity, because of its close relation to the liver, gall ducts, gallbladder, spleen, kidneys, ureters, urinary bladder, and, in women, internal genitalia, is liable to infection from diseases of these organs Infection of the peritoneal cavity is termed peritonitis Peritonitis is referred to as being present in the acute, localized, and chronic forms

Acute Peritonitis. Acute peritonitis may be either a primary or a secondary infection of the peritoneum

Acute primary peritonitis arises from the organisms, most frequently pneumococci, streptococci, or *Mycobacterium tuberculosis,* reaching the peritoneum by way of the blood or the lymph An *acute primary peritonitis* often occurs in infant girls, and in this form of the disease the pyogenic organism probably reaches the peritoneum through the genital tract Acute primary peritonitis is frequently observed as a terminal event in nephritis, arteriosclerosis with renal insufficiency, gout and other chronic diseases. This type of peritonitis may be associated with a terminal pneumonia and also in some instances with a pericarditis

Acute secondary peritonitis results from an extension of inflammation from the perforation of a hollow viscus which is covered by the peritoneum, such as the appendix, stomach and intestine, or from acute suppurative inflammation of the spleen, liver, pancreas, retroperitoneal tissues and pelvic viscera In this group of infections of the peritoneum is included the peritonitis which results from penetrating

wounds in the abdomen and from the rupture of normal graafian follicles, and the peritonitis occurring in the course of septicemia and following surgical operation.

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Acute secondary peritonitis always tends to *localize*, thus giving the symptoms of an abscess in the vicinity of its localization However, localized or circumscribed peritonitis may change into acute generalized peritonitis

The symptoms of localized peritonitis depend on the situation of the infected organ which is producing the peritonitis Since localizing peritonitis more often is produced by appendicitis or pelvic abscess than by other causes, it is most frequently situated in the right iliac fossa and in the pelvis

In women the commonest causes of pelvic peritonitis are puerperal septicemia, gonorrhea and tuberculosis of the internal genitalia In these conditions there are signs of a localized peritonitis or abscess in the pelvis

DIAGNOSIS. The diagnosis of a generalized, or a localized, primary or secondary acute peritonitis depends on obtaining the history and observing the afore-mentioned findings

Subdiaphragmatic Abscess. In 3 of every 4 instances collection of pus *under* the diaphragm is due to rupture of an abdominal viscus, or soiling of the *peritoneum* during surgical operation. In 1 of every 6, there has been an *extension from an* adjacent abscess, such as a perinephritic abscess. In the remainder the *infection* is blood borne from a distant focus In about one third of the cases the abscess *follows* appendicitis and in from one fourth to one fifth of the cases the abscess has developed subsequent to perforation of a peptic ulcer

Pleural effusion of clear sterile fluid on the affected side is the commonest associated lesion of a subdiaphragmatic abscess

SYMPTOMS. Subphrenic or subdiaphragmatic abscess following surgical operation or perforation of a viscus is considered if symptoms suggesting a *severe infection* appear from 4 to 10 days after the perforation or operation. Usually the first symptoms are a rise in temperature, hiccough and a gradually increasing toxemia Pain may be present on the affected side in the thorax or in the upper part of the abdomen. Shoulder tip pain is not often complained of by the patient. Its presence *may* be admitted. Deep breathing accentuates the shoulder tip discomfort.

EXAMINATION On inspection, fullness of the intercostal spaces over the suspected lesion rarely is detectable Some bulging of the lower part of the thorax and limitation of thoracic motion on the diseased side may be present if the collection of pus is large An abscess in the left anterior fossa may cause a visible prominence below the left rib margin anteriorly and a smooth tender tumor may be palpable in that region In subphrenic collections of pus, jarring of the lower part of the thoracic cage may produce severe pain

On percussion, dullness is present at the base of the lung on the affected side because of elevation of the diaphragm. Hepatic dullness may extend as high as the *third or fourth interspace anteriorly or into the axilla. Diminished or absent* breath sounds together with impaired tactile and vocal fremitus are often present at the base of the lung There may be a friction rub In some hyperresonance may extend below the costal margin.

If gas and pus are present in the abscess, the breath sounds and voice sounds are amphoric.

DIAGNOSIS. The diagnosis of a subdiaphragmatic abscess requires a knowledge of the history, the physical findings and roentgenologic examination A neutrophilic leukocytosis is revealed in the beginning of the infection if the patient's resistance remains good

Chronic Peritonitis. Since tuberculous peritonitis is so common, the criteria for diagnosis of chronic peritonitis are based largely on the presence or the absence of symptoms which may occur in this disease. However, there are, no doubt, many low-grade forms of chronic peritoneal infection which are evidenced by the presence in the abdomen of adhesions or fibrous bands which are not of *tuberculous* origin There may or may not have been symptoms of peritonitis These adhesions do not produce symptoms unless they are so situated that they interfere with the passage of the alimentary material through the lumen of the gut. In other words, unless adhesions or fibrous bands can produce obstruction of the intestine, other causes for abdominal symptoms should be sought.

Tuberculous Peritonitis. Tuberculous peritonitis occurs in adolescence or early adult life The disease in children before puberty attacks the sexes equally. Among children less than 2 years of age the disease is rare, and among persons more than 40 years of age the incidence again diminishes After this period the greater incidence is among women. Tuberculous peritonitis may be either acute or chronic.

In the severe forms of acute tuberculous peritonitis there are fever, chills, sweats, tachycardia and cyanosis These symptoms may be so severe that the *peritoneal* involvement is not appreciated unless the abdominal distention becomes *prominent* In the less severe acute stage of tuberculous *peritonitis the disease* commences *with*

generalized abdominal pain, nausea, vomiting, gaseous distention and a rapid accumulation of ascites.

When there is an active tuberculous focus in the abdomen or pelvis, such as a tuberculous mesenteric lymph node, a tuberculous intestine or a tuberculous uterine tube, at first there may be symptoms of localized peritonitis in the region of the infected part Then there may appear an acute abdominal condition which may indicate a miliary involvement of the peritoneum The symptoms of these miliary tuberculous processes extending from a primary focus in the abdomen are such that an acute secondary peritonitis is suspected After the acute symptoms subside, plastic masses of adherent and thickened intestine form and become palpable. The clinical course is then subacute or chronic, with remittent fever, sweats and emaciation

The commonest source of chronic tuberculous peritonitis appears to be tuberculous mesenteric nodes—the so-called tabes mesenterica The bovine strain of the tubercle bacillus is the usual offender in cases of tabes mesenterica.

The *pathologic changes* in the peritoneum are comparable to those of the pleurae when infected by tubercle bacilli. Just as there are a dry form and a wet form of pleurisy, there are the dry and the wet forms of peritonitis In association with the latter there is marked ascites. Examination of the peritoneal surfaces reveals the presence of tubercles In the dry form there is little effusion, but the peritoneal surfaces are adherent in places

The *symptoms* may comprise high fever and abdominal pain varying in intensity; occasionally there is a friction rub on respiration in a patient who has the dry form of the disease Despite widespread adhesions and fibrosis, intestinal motility is maintained well Intestinal obstruction does occur, but is not common

Examination will reveal that the patient is often emaciated The abdomen has been described as having a doughy feel The intestines may be matted together in a palpable mass The omentum may be thickened and drawn together by fibrosis to form a thick mass, which is palpable and may resemble a true neoplastic process.

Leukocytosis varies Often there is a slight increase in the total count, but polymorphonuclear leukocytosis is not present

If the intestinal lumen is deformed by an active tuberculous process, the roentgenologic examination may reveal characteristic changes which will establish the *diagnosis* In the absence of active tuberculous foci elsewhere, it may be necessary to perform surgical exploration to establish the diagnosis Some physicians use peritoneoscopy as a diagnostic procedure An exploratory operation is of low risk to the patient and has the advantage of obtaining tissue so that a definite diagnosis can be made by histologic study and by cultural means

Diseases of the Peritoneum Due to Higher Animal Parasites. Echinococcus disease of the peritoneum occurs as a part of this generalized infection There are present multiple abdominal tumors. The diagnosis of the disease is rarely made prior to surgical exploration and biopsy, or necropsy Rarely are the cystic forms of other worms observed

Tumors of the Peritoneum. Primary tumors of the peritoneum are rare. Metastatic tumors of the peritoneum are common in association with the terminal stages of cancer of the intraperitoneal organs Carcinomas of the ovaries and the stomach, colon and rectum are specially prone to cause widespread tumors on the peritoneal surfaces Often, when metastatic tumors are present in the peritoneum, ascites is present

Little can be done for patients who have metastatic tumors of the peritoneum Abdominal paracentesis may offer the only chance for temporary relief.

THE MESENTERY

Congenital Anomalies of the Mesentery. The normal distribution and position of the mesentery depend on the normal development of the intestines, rotation during embryonic life, and fixation or anchoring of the fully developed intestine. A total failure

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rarely attain a large size They tend to occur multiply. Mesocolic cysts are lined with endothelial cells and contain light yellow-colored fluid, and these may occur multiply Dermoid cysts may attain great size. They maintain their usual characteristics when present in the mesentery They usually occur singly.

The symptoms do not commence until the cyst is large enough to give pressure on, or obstruction to, the intestine In large cysts the appearance of a mass may be the only complaint In some instances the first symptom may be an acute abdominal emergency, such as intestinal obstruction, or volvulus, precipitated by the tumorous growth.

There is a tumor in the abdomen Rarely can fluctuation in the mass be obtained. The mobility of the tumor varies; some are highly mobile while others are ill defined in outline and of limited movement in the abdomen.

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operation The diagnosis of most mesenteric cysts is uncertain prior to surgical operation or necropsy

Solid Tumors of the Mesentery and Retroperitoneal Space. The solid tumors of the mesentery and retroperitoneal space may be either benign or malignant, and their variety is equal to the number of different types of connective tissue present in the mesentery and in the structures in and about the root of the mesentery and in the peritoneal regions

Lipomas or myxomas are the commonest solid tumors arising in the mesentery and are often multiple It may be difficult to determine whether fibromas and fibromyomas are extra-intestinal or arise from the bowel between the leaves of the mesentery. The malignant lymphomas, often of the Hodgkin type, are the commonest solid tumors arising in the retroperitoneal spaces.

Other tumors which frequently are found within the mesentery are metastatic growths, either carcinomas or those of the lymphoblastoma group, which includes Hodgkin's disease

There are no characteristic manifestations A tumor may or may not be palpable on examination. In Hodgkin's disease there may be fever of the Pel-Ebstein type and often superficial lymph nodes from which biopsy studies may be made. The solid tumors are diagnosed as tumors of the mesentery or retroperitoneal spaces on direct examination by the pathologist or surgeon

The prognosis depends on the type of tumor Benign tumors, particularly the lipomas of the mesentery, have a great tendency to recur

THE OMENTUM

The omentum varies greatly in size and, if large enough, is often at the site of intra-abdominal pathologic change, but its presence there is the result of being displaced from its usual resting place, the displacement having been initiated by such forces as peristalsis, diaphragmatic excursions, and changes in posture of its owner. Once the omentum is at the site of infection or injury, it may become adherent to the diseased tissue and become palpable

Diseases of the Omentum Due to Prenatal Influences. The congenital defects of the omentum comprise omental bands and omental cysts

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bands cause any symptoms, they are the result of angulation, trauma, and perhaps intestinal obstruction at these points.

In rare instances intestinal obstruction may have been present intermittently since childhood or since regular ingestion of a diet containing solid foods.

of fixation of the intestine permits excessive motility of the bowel, which may twist about the root of the mesentery, producing volvulus and obstruction. Segments of the mesentery may be long while others are short Both long and short mesenteries may be implicated in intestinal volvulus.

The primitive cavity of the omental bursae sometimes is not fully obliterated during prenatal life. In these instances the inferior recess may extend to the caudal end of the greater omentum.

Infections of the Mesentery. Mesenteric Lymphadenitis. This is an inflammation and enlargement of the mesenteric lymph nodes of the ileocecal region, the cause of which is unknown

The presence of soft, swollen, inflamed nodes in the ileocecal region may be accompanied by an increased amount of peritoneal fluid. On rare occasions the nodes may suppurate, and when this occurs, the findings are similar to those in cases of appendical abscess except for the fact that the appendix is normal

The disease usually occurs before adult life and is seen with increasing frequency after the third year. The symptoms consist of pain usually situated, and remaining, in the right lower quadrant of the abdomen Nausea is frequent; vomiting may occur Diarrhea is frequently present The physical examination does not reveal tenderness and the muscle rebound phenomenon There is often fever Leukocytosis may be increased out of proportion to the physical findings.

Appendicitis is usually the preoperative diagnosis. There is one important distinguishing feature between this disease and appendicitis· It is rare for the patient who has appendicitis to have diarrhea Constipation is the rule in appendicitis. However, acute appendicitis cannot always be excluded and therefore the correct diagnosis is made at surgical operation

The prognosis is uncertain. Symptoms may continue for a long time Eventual recovery is expected

Tuberculosis of the Mesenteric Lymph Nodes. This disease affects the two sexes with equal frequency.

Tuberculosis of the abdominal lymph nodes is often associated with tuberculous enteritis and frequently is fatal in infants and children In some patients this form of tuberculosis runs a mild course Often, when calcification of the lymph nodes is found later in life, there is no history to suggest that a tuberculous adenopathy was ever present. In those who have recovered from the disease, the calcified nodes remain in the mesentery and may interfere with the interpretations of intravenous pyelography at a later date

The ileocecal nodes are usually affected In an active tuberculous infection there are caseous nodes in the mesentery The extent of lymph-node involvement is more extensive in the presence of ulceration of the intestine by tubercle bacilli

The symptoms commence with pain situated in the middle of the abdomen The pain recurs two or three times a day and stops as suddenly as it starts Between attacks there is comfort The pain is generalized, but if unilateral, is more severe on the right side than on the left These symptoms recur at irregular intervals There may be nausea, vomiting, and constipation Physical examination does not reveal characteristic findings There may be tenderness in the right iliac fossa

The diagnosis is usually made at necropsy, or on biopsy of a lymph node removed at the time of an exploratory laparotomy. However, in those in whom there are no other serious foci, the prognosis is good

Cysts of the Mesentery. Aside from the cysts of parasitic origin (echinococcus), mesenteric cysts are largely of congenital origin They may be enumerated as (1) enterocystomas; remnants of the normal diverticula of the intestines pinched off from the intestines at an early embryonic age, (2) chylous cysts (lymphangioma cavernosum), (3) mesocolic cysts and (4) dermoid cysts.

Enterocystomas are lined with epithelial cells similar to the lining cells of the adjacent gut. They are the commonest mesenteric cysts Chylous cysts are small and

(atherosclerosis) and (4) mycotic aneurysms resulting from septicemias Periarteritis nodosa usually does not involve large arterial trunks. Trauma is rarely a cause of an aneurysm of the aorta.

Aneurysms of the descending aorta in those past 45 years of age are considered generally to be predominantly arteriosclerotic, syphilis being responsible for only 9 per cent in the series of abdominal aneurysms reported by Mills and Horton. However, in patients less than 45 to 50 years of age, among whom there are more Negroes than whites, syphilis is responsible for more than one half of abdominal aneurysms. Arteriosclerotic abdominal aneurysm occurs predominantly in those more than 60 years old and almost never before 45 years of age. The syphilitic aneurysm usually occurs at the level of the celiac axis

Aneurysms of the descending aorta may reach immense size and may almost completely fill the thoracic cavity or the abdomen before they produce symptoms. If the aneurysm arises in the thorax, there may be a huge thoracic mass discovered on roentgenologic examination of a patient who has complained of few or no symptoms If manifestations of aneurysms in the thoracic cavity are present, they consist of thoracic pain, dyspnea and cough. Dysphagia is an occasional symptom resulting from pressure on the esophagus There is a visible pulsation on the posterior thoracic wall either below and to the left of the left scapula or somewhat higher in the interscapular region

If the aneurysm of the aorta is situated within the abdominal cavity, it is manifested by pain in the abdomen and the back The pain may be paroxysmal, or constant and boring There may be root pains extending from the back to the upper part of the abdomen These and other symptoms result from erosion of the vertebrae and pressure on the spinal cord, gastrointestinal tract, ureter or other abdominal structures. Death is usually caused by rupture of the sac into the peritoneal cavity, gastrointestinal tract or retroperitoneal space. In the experience of Estes only one third of those who have abdominal aneurysms have symptoms at the time the diagnosis is made or suspected

The diagnosis is established by the presence of a pulsating expansile abdominal tumor. The roentgenologic and roentgenoscopic examinations confirm the impression gained by physical examination. The roentgenologic examinations reveal opaque shadows caused by atheromatous plaques throughout the mass. Aortography is a precise diagnostic procedure.

Aneurysm of a *renal artery* etiologically has the same origin as aneurysms of the thoracic and abdominal aortas The so-called *false aneurysm* results from trauma to the renal artery, a vessel which may have been weakened by a congenital fault The cardinal symptoms of false aneurysm are hematuria, pain and tumefaction in the flank. Pulsation and a systolic bruit may be present The presence in the roentgenogram of a ringlike shadow in the renal region, with a dense periphery disrupted in one portion and a rarefaction of the center, is suggestive of aneurysm of a renal artery

A *true aneurysm* of a renal artery is usually asymptomatic. It is found by palpation of the abdomen If symptoms are present, they arise from pressure or from pain which may have the characteristics of renal colic. On examination a palpable, expansile, pulsating mass may be present The diagnosis is established by roentgenologic methods However, aneurysms of the renal arteries usually are not diagnosed prior to surgical exploration or prior to death.

Aneurysm of the *splenic artery* usually is not diagnosed prior to operation or to death The aneurysm usually is asymptomatic until the time of rupture. Before rupture there are complaints which vary from mild epigastric pain to more severe abdominal complaints which may suggest gallbladder disease or peptic ulcer Pressure of the aneurysm on the pancreas may cause insufficiency of the external secretions of the pancreas manifested by steatorrhea. The spleen is palpable owing to infarction. In some, a pulsation may be felt or a bruit heard in the left upper part

The diagnosis is made at the time of surgical exploration of the abdomen or at necropsy.

Omental Cysts. A great many omental cysts, including dermoid cysts, are no doubt of congenital origin. The source of the rest of them is obscure.

Intestinal obstruction or torsion of the omentum may occur in association wit omental cysts. In large cysts, abdominal tumor is present. In such cases ascites ma be impossible to differentiate.

Cysts are diagnosed clinically as abdominal tumors. The nature of the tumo awaits direct inspection Discovery by roentgenologic examination of the presence o *calcium in the cyst may suggest the diagnosis Dermoid cysts are definitely diagnose* roentgenographically

Cysts of the mesentery and peritoneum, cysts of the retroperitoneum, splenic hepatic and renal tumors, and aneurysm may not have any clinical differential diag nostic features from those of omental cysts.

Diseases of the Omentum Due to Trauma or Physical Agent. *Torsion of the Omentum.* Omental torsion occurs on the long axis of the omentum The condition is incident to the fourth and fifth decades of life, and men are affected twice as frequently as women Two thirds of all instances of omental torsion occur in inguinal and scrotal hernias of long duration Almost all are on the right side of the abdomen with the right lower quadrant the site of the torsion

The existence of torsion of the omentum may be attributed to adhesions, to inflammatory omental foci following subsiding acute intra-abdominal inflammatory lesions, and to a fat omentum

The peritoneal reaction usually produces a sanguineous ascites Most often there are signs of a pre-existing pedicle, and occasionally the pedicle may rupture and the mass become parasitic on the peritoneum or on a viscus Usually only a portion of the omentum in the right lower abdominal quadrant is affected, although the entire omentum may be strangulated.

The onset of symptoms is by a sudden acute, severe abdominal pain in the right lower quadrant High fever, fast pulse and increased respiration quickly ensue In some cases vomiting is intractable, in others it may be absent. On examination by the time the symptoms have become established, there is a tender abdominal tumor. The tumor, at first, is not well delineated, often owing to muscle guarding. The muscles soon become rigid Leukocytosis is present.

The diagnosis is made at the time of surgical exploration Prognosis is good when early surgical treatment is instituted.

Infarction of the Omentum. Inspection reveals necrosis and hemorrhagic extravasation into the omentum There is no suggestion as to the origin of the condition The symptoms and signs are those of the "acute abdomen" which require several days for development The condition has not been diagnosed preoperatively or prior to death The prognosis is not good despite early surgical treatment.

Solid Tumors of the Omentum. Solid tumors of the omentum are the same as those occurring in the mesentery, for the origin of the omentum is comparable with that of the rest of the mesentery

ANEURYSMS OF THE DESCENDING AORTA AND THE ABDOMINAL VESSELS

Abdominal aneurysms arise from the descending aorta (made up of the thoracic and abdominal aortas) or from main arterial branches which are extended to the principal abdominal organs; for instance the renal, the splenic, the hepatic and the iliac arteries. Moreover, dissecting aneurysms may arise in any part of the thoracic aorta and extend downward and give rise to symptoms referable to the abdomen.

Abdominal aneurysms etiologically result from (1) congenital defects in the artery, (2) syphilitic infections involving the aorta, (3) atheromatous changes in the vessels

the peritoneal cavity The swelling increases and the wall of the bowel becomes thickened until the lumen is obstructed. Ischemic necrosis often ensues.

The symptoms commence with sudden severe generalized abdominal pain, diarrhea, bloody stools and often shock The diarrhea continues until a general peritonitis is established and the abdomen becomes silent The pain usually remains generalized. Vomiting is continuous, and finally there is fecal vomiting. Neither the expulsion of vomitus nor the passage of flatus gives any relief from the distention of the abdomen or the pain.

The diagnosis is usually made at laparotomy or necropsy. Pancreatic hemorrhage, intestinal strangulation, perforated ulcer, and a twisted tumor pedicle all symptomatically resemble mesenteric thrombosis.

The disease is almost universally fatal Whether or not recovery from the occlusion ever occurs cannot be stated because of a lack of objective diagnostic data. Occasionally extensive resections of the infarcted bowel have been followed by survival of the patient

Abdominal Apoplexy (Rupture of a Mesenteric Blood Vessel). Abdominal apoplexy is a rare intra-abdominal emergency Atherosclerosis with or without aneurysmal formation is responsible for the spontaneous rupture of an artery in the abdomen. The gastric and superior mesenteric arteries usually are the ones that rupture Men are affected twice as frequently as women

In contradistinction to its counterpart, cerebral apoplexy, which may occur again and again, abdominal apoplexy rarely recurs Usually this catastrophe is fatal; an occasional patient has survived. There has never been a proved preoperative diagnosis.

ABDOMINAL EPILEPSY

Moore defined abdominal epilepsy as a disorder characterized by paroxysms of acute abdominal pain The pain is due to hypermotility of the bowel, provoked by abnormal discharges of certain neurons in the vicinity of biochemically or structurally altered cerebral tissue, presumably situated in the premotor and postmotor cerebral cortex or the diencephalon

An area of the brain just posterior to the postcentral convolution when stimulated gives pain in the abdomen like that which some patients experience before epileptic attacks Stimulation in front of this region reproduces typical epileptic seizures Patients may experience intense abdominal pain as the initial symptom of a cerebral hemorrhage Klingman reported observations on 12 children who had paroxysmal attacks of abdominal pain. The electro-encephalographic anomalies in all these were suggestive of cerebral dysrhythmia In 9 of the children neurologic symptoms consistent with convulsive disorder developed afterward Some of them remained free of symptoms under anticonvulsant therapy

In a study of 14 cases of abdominal epilepsy by Moore about half of the patients had a history of brain injury as a suggestive, and in some cases as an undoubted, relationship to the onset of abnormal cerebral discharges and the symptoms of paroxysmal abdominal pain The majority of these patients had been treated for a variety of abdominal conditions or had received treatment, equally futile, for psychoneurosis The great majority of these patients obtained relief from anticonvulsant therapy

The criteria for diagnosis are based on (1) exclusion of intrinsic visceral disease, (2) a history of attack the pattern of which is of an epileptic order and (3) objective evidence of cerebral organic disease or dysfunction

ABDOMINAL MIGRAINE

Many patients who have migraine headaches have regularly, with each headache, nausea and vomiting, and some have vomiting without headache. Still others

of the abdomen and thus may suggest the diagnosis. Roentgenologic examination may reveal calcification in the wall of the aneurysm, as an oval shadow with the periphery sharply delineated and the central portion presenting a mottled appearance.

In Long's series of 44 cases of aneurysms of the *iliac arteries*, the ages of the patients ranged from 40 years to 80 years with the greatest age incidence past 70 years. The disease was commonest in men The aneurysms which were present in the 3 women were asymptomatic. In this series the cause of aneurysm formation appeared to be arteriosclerosis in all instances In 4 of Long's cases the aneurysms produced symptoms of urinary and intestinal distress and caused the deaths of the patients by rupture with exsanguination The duration of symptoms varied from 11 days to 5 months before death In 40 cases the aneurysm was found incidentally at necropsy.

Aneurysm of the *hepatic artery* is exceedingly rare. The symptoms, when present, consist of pain in the right upper quadrant of the abdomen, jaundice, and evidence of bleeding into the alimentary tract Aneurysm of the hepatic artery is diagnosed at the time of surgical operation or more commonly at the time of postmortem examination.

Dissecting Aneurysm of the Descending Aorta. A dissecting aneurysm of the descending *thoracic aorta* produces pain in the thorax which may extend to the abdomen However, in most instances of dissecting aneurysm, when pain becomes manifest it is acute and severe and must be differentiated from that due to myocardial infarction

A dissecting aneurysm of the *abdominal aorta* begins insidiously and has a prolonged course. The illness is characterized by abdominal pain in the course of the abdominal aorta or its branches. The pain is often severe but is characterized by remissions during which there is only a dull ache present Dissecting aneurysms of the abdominal aorta may be suspected, but usually they are diagnosed at the time of necropsy unless an aortogram is made

Aneurysms may occur in the vessels of the hollow viscera, for instance the stomach or the colon They may rupture and cause severe hemorrhage, manifested by hematemesis or melena and shock The diagnosis of these lesions usually is made at the time of surgical exploration to discover and to correct the cause of the hemorrhage unless an aortogram has been made

OCCLUSIONS AND RUPTURES OF THE MESENTERIC BLOOD VESSELS

The mesenteric blood vessels may be the site of occlusion or rupture The etiology in both conditions is usually an atherosclerosis.

Mesenteric Vascular Occlusion. Mesenteric vascular occlusion occurs in aging persons.

Atherosclerosis is the most important contributing cause of mesenteric vascular occlusion. Occlusion of the mesenteric vessels sometimes follows abdominal and pelvic operations, particularly appendectomy.

Arterial occlusion results from either embolism or endarteritis Endarteritis causes a slow occlusion Men are affected more often than women

The superior mesenteric artery is most commonly occluded It is for this reason that in mesenteric occlusion the greater part of the jejunum and the ileum, and often the cecum and the ascending colon, are affected. In occlusions of the superior mesenteric artery there can be but meager development of collateral circulation, for this vessel behaves like an end artery when occluded The degree of involvement of the bowel depends on the size of the branch occluded and on the accompanying vasospasm The occlusion of either a mesenteric artery or a vein acts the same in regard to the amount of congestion of the bowel In either case congestion is the main feature The extravasation of blood which follows initiates peritoneal irritation, and free fluid accumulates in

urine rapidly ensue When the condition is severe, extreme dehydration, hypochloremia and alkalosis occur.

On examination visible gastric peristalsis is often present. Direct percussion over the stomach may initiate the peristaltic waves. A small, firm, smooth palpable tumor in the pyloric region is usually present. This tumor is best palpated when the child is asleep or while nursing before the stomach is filled Roentgenologic examination is diagnostic.

The rarer anomaly, congenital atresia of the *duodenum*, may closely simulate the symptoms of congenital stenosis of the pylorus In congenital atresia the narrowing of the bowel is in the second part of the duodenum No tumor is palpable in the epigastrium Roentgenoscopic examination reveals a complete obstruction. Duodenal atresia cannot be differentiated from congenital pyloric stenosis if the atresia is close to the pylorus The manifestations of congenital hyperplasia of the adrenal glands may closely resemble those of hypertrophic pyloric stenosis.

Hypertrophy of the Pyloric Muscle in Adults. The variation in the thickness of the pylorus in normal persons depends on the size and age of its owner. Horton admitted great difficulty in determining the actual normal size of the pylorus.

Hypertrophy and thickening of the muscle fibers of the pylorus are a very rare cause of symptoms and signs of pyloric obstruction in adults In affected adults the hypertrophy of the pyloric musculature is identical with that in hypertrophic pyloric stenosis of infancy. The condition in adults is perhaps the result of residual low-grade congenital pyloric stenosis Any other postulation is beset by the vagaries of subjective symptoms as recorded in routine history writing

Some patients have gastric symptoms and periodic attacks of vomiting which date from infancy In others there may be vague and indefinite symptoms which began, so far as the patient knows, in adult life In late or middle life some of those who are proved to have hypertrophic pyloric stenosis have symptoms, of brief duration, which resemble those of peptic ulcer and pyloric obstruction The history may be short, the symptoms progressive and the stomach achlorhydric

A positive diagnosis of hypertrophy of the pyloric muscle in adults is possible by a trained roentgenologist.

Cascade Stomach. In the cascade stomach the posterior wall of the pars cardiaca is not in the same plane with the pars media, which is anterior to its normal position, the greater portion of the vertical limb of the stomach being displaced forward The roentgenologist records that on ingestion of a small amount of barium, the barium passes and fills the pars cardiaca before it enters the pars media and the pars pylorica. Suddenly then the barium fills the pars pylorica

Cascading does not cause either subjective or objective complaints; however, like other minor congenital anomalies, it predisposes toward gastric dysfunction when the stomach is otherwise adversely affected.

Volvulus of the Stomach. The most important predisposing causes of gastric volvulus are congenital ptosis or marked relaxation of the ligamentous supports of the stomach Tears in the gastrocolic and gastrohepatic omenta permit of volvulus The spontaneous occurrence of volvulus of the stomach is aided by disorders of the diaphragm, for instance, diaphragmatic hernia, or eventration of the diaphragm, or by left phrenicectomy The intragastric causes of volvulus are hourglass stomach, gastric ulcer, malignant lesion at the cardiac end of the stomach, benign tumors of the stomach, acute dilatation of the stomach and excessive antiperistaltic movements

The symptoms are similar to those of the other acute conditions in the upper part of the abdomen A clinical preoperative diagnosis is not made

The prognosis depends on the surgical skill available and the length of time elapsed before surgical operation is performed.

Diverticula of the Stomach. Four gastric diverticula were found by Rivers, Stevens and Kirklin in 3,662 subjects of routine necropsy.

Gastric diverticula are classified as (1) true (probably congenital) and (2) false or

have nausea, vomiting and abdominal pain occurring with the headache. In a few of those who have migraine, nausea, vomiting and abdominal pain will occur without cephalalgia In this last named group the condition has been termed abdominal migraine.

THE STOMACH

The pylorus lies in the median line 1 to 2 inches (2.5 to 5.1 cm.) below the tip of the xiphoid or ensiform cartilage, when the stomach is distended, the pylorus moves 1½ to 2 inches (3 8 to 5 1 cm.) to the right. The lower border of the stomach crosses the median line 2 to 3 inches (5.1 to 7.6 cm.) above the umbilicus.

Percussion In physical diagnosis the size of the stomach may be outlined approximately by percussion, if it is filled mainly by air or gas However, if the stomach is filled mainly by liquids, as is often the case in pyloric obstruction, the outlines cannot be found by percussion

Traube's semilunar space is limited above by the edge of the left lung, indicated by the sixth interspace, externally by the spleen, indicated by the midaxillary line; and internally by the costal margin. Pleural effusion causes this space to be dull on percussion The diagnostic value of this sign has great limitations, owing to its variability

Lymphatic Structures The inferior lymph nodes of the stomach are found principally around the regions of the pylorus, and the superior gastric nodes around the lesser curvature and cardial extremity The inferior nodes drain the greater curvature toward the pylorus, while the superior nodes drain the lesser curvature and cardial end The fundus is drained by radicles which empty into the nodes which accompany the splenic artery Some nodes may be found along the greater curvature toward the pyloric end It is rare to find nodes in the middle portion of the greater curvature and quite exceptional to meet with them in the region of the fundus. In cancer of the stomach these nodes do not become palpable until late in the disease if at all.

Diseases (Anomalies) of the Stomach Due to Prenatal Influences. Absence of the stomach (agastria), doubling of the stomach and accessory stomach have been recorded There are congenitally small and congenitally large stomachs The greatly enlarged stomach is often accounted for by the presence of hypertrophic pyloric stenosis or duodenal atresia Actual developmental megalogastria probably occurs

A congenitally right-sided stomach is present with general transposition of viscera A failure of normal rotation of the foregut accounts for the presence of the stomach above the liver on the right side. This anomaly is compatible with normal digestion and health The situation of the stomach when associated with eventration of the diaphragm may resemble hydropneumothorax. Complete inversion of the stomach characterized by the orad position of the greater curvature together with a left lateral position of the cardia is rare In such a stomach the duodenal cap is directed downward and the transverse colon often angulates in its midportion.

Congenital Hypertrophic Pyloric Stenosis. Congenital hypertrophic pyloric stenosis is occasionally observed in otherwise healthy infants. The sex ratio is approximately 4 boys to 1 girl Several members of the same family may have the anomaly.

There is hypertrophy of the pyloric musculature. In many instances the degree of organic constriction of the pyloric lumen is insufficient to cause complete obstruction and there is an additional element of spasm. The thickening of the pyloric musculature accounts for the oval, firm tumor The gastric wall in the prepyloric region may be thickened and some dilatation of the stomach may be present. Simple hypertrophy of the pyloric muscle in the adult is most likely the result of this congenital anomaly.

The symptoms usually commence during the second week after birth but may be delayed to a later age There is regurgitation which progressively increases until supplanted by periodic spells of vomiting The child does not vomit after each feeding, but after several feedings have accumulated, and will promptly resume nursing immediately after the vomiting In the severely obstructed pylorus the vomitus is free from bile Loss of weight, constipation, and decrease in the quantity of

have revealed streptococci and, in some cases, staphylococci, colon bacilli and pneumococci There is diffuse suppurative infiltration of the submucosa with thickening of the walls A localized abscess may rupture into the stomach or into the peritoneum.

The important symptoms are pain, high fever, vomiting, dry tongue and dehydration and occasionally jaundice The vomitus contains pus. Occasionally there is a tumor which can be palpated.

The prognosis is grave The diagnosis rarely is made before death because the patient is too ill to be examined roentgenologically or endoscopically.

Acute Gastritis of Toxic Origin (Exogenous Gastritis) This disease is initiated by swallowing of chemical, thermal, mechanical or bacterial irritants. Common examples of these irritants are alcoholic beverages and medicines, such as salicylates, ammonium chloride, quinine, creosote, coal-tar products, iodides and bromides, administered either in large doses or to hypersensitive subjects. Mechanical distention brought about by eating too much, rarely, if ever, causes an inflammatory reaction in a stomach. A combination of alcoholic drinks and gluttony, however,

Endoscopic examinations are not permissible during or immediately following an episode of acute exogenous gastritis Observations of the interior of the stomach through fistulas of living persons do not contribute much to the understanding of this form of gastritis A fistulous stomach is not normal

Epigastric burning and distress of varying intensity, nausea, salivation, anorexia, vomiting, diarrhea, and disagreeable taste in the mouth are the common symptoms. In the more severe disorders, particularly if associated with diarrhea, there may be present extreme prostration, weakness and intractable nausea and vomiting. The vomitus contains much mucus If vomiting is protracted, the vomitus eventually consists of bile Hydrochloric acid may or may not be present in the gastric contents. A temporary suppression of acid secretion may occur during the acute phases of the disorder.

The general examination is informative mainly because of the negative evidences of systemic disease or other abdominal disease.

Acute (exogenous) gastritis may be suspected of being the cause of the forementioned symptoms if accompanied by a history of ingestion of a causative agent. Reflex symptoms resulting from trauma, migraine and acute abdominal diseases are always considered

Acute Corrosive Gastritis Corrosive gastritis results from the swallowing of organic acids (carbolic) or mineral acids or alkalies, or such poisons as phosphorus, bichloride of mercury or insecticides, ammonia, arsenic, and comparable substances. The most frequent causes of corrosive gastritis are lye, bichloride of mercury, carbolic acid and lysol (see Chapter 19)

With the noncorrosive poisons the pathologic process in the stomach consists of acute degeneration of the glandular elements and hemorrhage. With strong poisons the mucous membrane is destroyed extensively and may be converted into a brownish black eschar. In less severe grades of toxic gastritis, there may be regions of necrosis surrounded by inflamed tissue, and the submucosa is hemorrhagic and infiltrated

The first symptoms are feelings of strangulation, intense burning pain in the mouth, throat and stomach, salivation, great difficulty in swallowing, and constant vomiting which follows immediately. The vomitus is bloody and sometimes contains portions of the mucous membrane

The primary immediate concern in most of these cases is with the symptoms of the systemic poison and the administration of the appropriate antidote (see Chapter 19).

If a mild corrosive poison has been swallowed, the examination does not reveal significant findings; if a strong corrosive substance has been ingested, there will be

acquired. The occasional occurrence of concomitant diverticula in the duodenum and in the colon is further evidence that the true diverticula are due to prenatal influences The pouches frequently are situated in the posterior wall near the lesser curvature distal to the entrance of the esophagus. They may occur in other parts of the stomach including the pylorus True diverticula of the stomach may contain ectopic (pancreatic) tissue

Acquired diverticula are subdivided into the pulsion and traction varieties. The origin of these is ascribed to such vagaries as increased intragastric pressure, adhesions, and what not

Gastric diverticula are single and rarely exceed ⅘ inch (2 cm) in diameter. Retention in the pouch may occur when the stoma of the pouch is small.

Gastric diverticula are found accidentally by the roentgenologist in patients of any age Generally they are asymptomatic The symptoms if present are usually best accounted for by independent accompanying lesions of the esophagus, stomach, duodenum, or gallbladder Asymptomatic massive hemorrhage has been recorded, but unfortunately for the hypothesis for diverticular hemorrhage, these patients also have had peptic ulcer of the duodenum. If hemorrhage does occur it probably arises from ectopic tissue in the diverticulum The diagnosis is established by roentgenologic examination

Diseases of the Stomach Due to Bacteria and Those Due to Corrosives and Intoxication. Infections of the stomach exist in both acute and chronic forms. An acute or chronic gastritis may be caused by infection by lower plant and animal parasites or may be due to the effects of trauma from the poisonous corrosive effects of many and varied substances Often a gastritis arises from unknown causes.

Acute Gastritis. *Acute Infectious Gastritis* The stomach is peculiarly refractory to the direct invasion of bacteria unless the mucous membrane has been injured Infectious gastritis has been described in association with acute systemic diseases such as diphtheria, scarlet fever, pneumonia and other infections In these infections the lower organisms are carried through the blood stream to the stomach, where either the bacteria or their toxins are spread to the walls of the stomach.

SYMPTOMS The symptoms, if there is fever, are similar to the initial symptoms of many infectious diseases If an intense headache and delirium are present, the illness may resemble meningitis, or if the abdominal pains are intense, the attack may resemble gallstone colic or appendicitis

In the mild acute form of gastritis there are anorexia, vomiting, and dyspeptic symptoms which frequently accompany any acute febrile illness. In the course of the attack the temperature reaches 102 to 103 F (38 8 to 39 4 C) The average duration of the attack is 1 day, but it may last 3 days and occasionally longer. There is usually constipation; however, diarrhea may be present In severe gastritis of sudden onset, with chill and fever, the symptoms are like those of a severe infection. During the course of such systemic diseases as diphtheria, scarlet fever, and pneumonia there may develop an acute gastritis

On examination the tongue shows the effects of dehydration, a finding never missed by physicians of former times. Herpes may appear on the lips The abdomen may be somewhat distended and tender in the epigastric region

At first the substances ejected from the stomach contain food; later, bile-stained fluid and much mucus Examination of the vomitus reveals, as a rule, absence of hydrochloric acid and presence of lactic and fatty acids Leukocytosis (up to 15,000 leukocytes per cubic millimeter of blood) may be present.

The diagnosis is inferred if the illness clears within a few days If the symptoms do not clear, a gastroscopic examination will result in a correct diagnosis. The finding, however, of an acutely inflamed mucosa of the stomach may not mean that the patient has acute gastritis only There may be an acute systemic infection also

Acute Suppurative or Purulent Gastritis Acute suppurative gastritis may be a complication of either bacteremia or ulcer of the stomach. Young men are affected more frequently than women. Microscopic examinations of extirpated gastric tissue

om postoperative complications due to any type of general anesthesia Achlorydria, avitaminosis (vitamins B and C), allergic disorders, *Giardia lamblia*, and ichobezoars and phytobezoars are likewise suggested as causes for chronic gastritis

Ulcerative Gastritis. Severe ulcerative gastritis is a rare complication of chronic uodenal ulcer but when present may become constantly accompanied by symptoms. : is one cause of an inability to control peptic ulcer by medical treatment

Postoperative Gastritis Severe gastritis in the stomach that has been operated n is usually irreparable unless the gastroenterostomic passage is discontinued However, the prognosis for patients who have mild postoperative gastritis is decidedly iore hopeful than it is for those who have severe hypertrophic or atrophic forms f the disease

Up to this point the various forms of gastritis which have been considered have ome sort of an etiologic assignment. The possible causes of chronic gastritis have een enumerated Before proceeding, it is necessary to amalgamate these possible rigins and simply to state that they may cause either hypertrophic, atrophic, or form of mixed chronic gastritis; any one or all may arise from the etiologic agents vhich have been enumerated. In other words, the individual reaction to a stimulus annot be forecast

Hypertrophic Gastritis Hypertrophic gastritis is characterized by the tendency oward thickening of the mucosa and other layers of the gastric tissues, especially oward the pyloric segment, in which the changes may be limited

The sex incidence corresponds to that of duodenal ulcer, which is commoner n men than in women Hypertrophic gastritis may occur at any age.

Pollard and Cooper selected 50 patients who had hypertrophic gastritis who vere entirely free of any other evidence of organic disease, to determine whether or not they presented any consistent clinical symptoms as a result of their disease. The features which were commonly present and which should serve as a diagnostic aid were a burning sensation or discomfort in the epigastrium before, immediately after, or in about 2 hours after eating The discomfort was at times relieved by food or sodium bicarbonate Free acid in the gastric contents in normal or increased amounts was common However, generally the symptoms of this condition which can be assigned to pathologic findings occur in association with other diseases or with a condition produced by the gastritis which is similar to another disease, for nstance peptic ulcer

The time and situation of the pain may be those of a peptic ulcer, but the relief of pain by ingestion of food and antacids is often lacking The slightest dietary indiscretion provokes an exacerbation of symptoms Usually the appetite is not decreased, but loss of weight is definite because of dieting and sitophobia With the exception of hemorrhage, complications are comparatively rare Hemorrhage may be decidedly a prominent symptom in hypertrophic gastritis Intestinal symptoms, abdominal cramping and diarrhea are rare

Hypertrophic gastritis and peptic ulcer may be associated, a state which is revealed by gastroscopic examination The roentgenologic examination will reveal no definite diagnostic evidence of the disease When the symptoms of duodenal ulcer progress to the stage at which there is no remission of the suffering, the presence of hypertrophic gastritis is one of the complications which can create such a predicament

Hypertrophic gastritis after gastroenterostomy is not a frequent cause of the symptoms following anastomotic operations The symptoms of postoperative gastritis cannot be distinguished from those of peptic ulcer. They may be temporarily relieved by bland food or alkalies, but usually such relief is short-lived

In postoperative gastritis the questions always arise as to whether the patient had the gastritis before the operation and whether the gastritis failed to heal after the operation. The chances are that the gastritis existed prior to the operation.

evidence of the poison on the lips and in the mouth unless the poison was sipped through a quill or straw The patient often presents evidences of both physical and mental agony The abdomen is tender, distended and painful on pressure. The signs of shock or collapse and, sometimes, convulsions may be present. If the patient is examined a day or two after the ingestion of the poison, there may be petechiae in the skin and blood in the urine When the poisoning is less intense, there are sloughs in the mouth and gullet which may separate, leaving infected ulcers which may heal or which may lead to death from perforation, infection or exhaustion

The diagnosis of toxic gastritis usually is easy, as inspection of the mouth and pharynx reveals, in many instances, corrosive effects An examination of the vomitus may indicate the nature of the poison

Chronic Gastritis. *The term chronic* gastritis has become established despite strong argument against it The terms hyperacid gastritis and anacid gastritis are used to designate whether the gastritis is accompanied by hyperacidity or by anacidity. Pyloric gastritis, antral gastritis, fundic gastritis and pangastritis are used to indicate the situation of the more obvious changes as detected by gastroscopic or roentgenologic study.

Gastric function in all types of gastritis is so irregular and equivocal that it cannot be the basis of classification Schindler h [illegible] convincing proof of the frequency and significance of [illegible] to superficial, atrophic and hypertrophic varieties [illegible] chronic gastritis has been established by a method of taking biopsies from the gastric wall without ligatures or clamps If a normal mucosa is found gastroscopically, a normal histologic appearance of the biopsic tissue is expected

In this discussion of gastritis etiologic factors will be emphasized when known or suspected

The etiologies of chronic infectious gastritis in adult life may depend on an initial damage to the gastric mucosa resulting from acute infectious diseases contracted in childhood Many acute infectious diseases (due to bacteria, viruses or fungi) may damage the mucosa of the stomach to a degree which will permanently impair its secretory function and thus originate a chronic gastritis

In chronic infectious gastritis the symptoms are vague and indefinite. The findings on physical examination as well as the roentgenologic examination are characterized by an absence of positive evidence The diagnosis is established by endoscopic examination.

Chronic Irritative Gastritis Chronic gastritis may arise from the ingestion of gastric irritants For instance, injury to the gastric mucosa may follow an acute irritative gastritis initiated by concentrated alcohol or other corrosive agents or by food poisoning

Gray and Schindler concluded, after examining 100 men who had consumed an average of 2.8 pints of alcohol daily for more than 20 years, that the stomachs of 55 per cent were essentially normal In 45 per cent who had gastric disease it consisted mainly of superficial gastritis, atrophic gastritis or a combination of the two

No correlation was observed between the incidence and severity of the gastritis and the duration of the alcoholism, the amount of alcohol drunk, the use of nicotine, dental infection or vitamin deficiency. Why the drinking of alcohol is accompanied by severe and extensive gastritis in some cases and not in others is difficult to understand.

A long list of suspected substances which have had their protagonists as the cause for chronic gastritis may be enumerated, such as infected saliva, tobacco (chewed, dipped or smoked), drugs and condiments (particularly pepper) It is known that in heart failure and uremia there may be a stasis of blood in the gastric wall which may eventuate in gastritis Some gastritis almost always accompanies pyloric and duodenal obstruction. Gastritis may follow gastroenterostomy or result

membrane is grayish green This same mucosal appearance has been described in cases of pernicious anemia

Roentgenologic examination is essential to the diagnosis of gastritis in the same way that a general physical examination is essential Its value is in ruling out circumscribed lesions, particularly peptic ulcer, carcinoma and hiatus hernia.

All gradations in gastric acidity determined by analysis of gastric contents may be found in conjunction with all types of chronic gastritis. In diagnosis the determination of acidity has no value, in therapeusis the determination of gastric acids is helpful If there is a definite trend in values for gastric acid in cases of chronic gastritis, that trend is downward

Diagnosis of Chronic Gastritis. A clinical diagnosis of chronic gastritis is made only by exclusion The diagnosis, however, depends on the gastroscopic findings There is danger of attaching too much significance to minor aberrations from the normal mucosal image as viewed by the gastroscope

The most serious complication of hypertrophic gastritis is development of pyloric obstruction or severe hemorrhage from erosions and ulcerations In severe hypertrophic gastritis the lesions never heal completely even though the patients may become symptom free Carcinomatous change is not to be anticipated in hypertrophic gastritis, nor does hypertrophic gastritis eventuate in atrophy of the gastric mucosa.

Those who have atrophic gastritis are prone to development of severe hypochromic anemia, pernicious anemia or gastric malignant lesions

Epidemic Nausea. Epidemics of nausea have been recorded from time to time It seems that the maximal epidemic curve occurs in the autumn of the year. The incubation period appears to be less than one week The disturbance sets in suddenly with violent nausea and vomiting together with dizziness resembling motion sickness, and is over in a day or two There is no abdominal pain or diarrhea. The cause is unknown but a viral etiology has been suspected

Tuberculosis of the Stomach. Tuberculosis of the stomach is rare. The disease occurs oftener in men than in women Primary invasion of the stomach accompanies pulmonary tuberculosis and acid-fast lesions in the abdomen or the pelvis, or in the bones, epididymides, kidneys or other parts of the body In rare instances the tubercle bacilli may directly invade the gastric mucosa by entrance into a nonspecific lesion in the stomach such as a malignant tumor or a peptic ulcer.

Broders described the various pathologic manifestations of gastric tuberculosis They include single or multiple ulcers, miliary tubercles in association with a generalized miliary tuberculosis, solitary tubercles, pyloric stenosis, tuberculous nodules, and tuberculous lymphangitis The ulcerating gastric lesions are the commonest The ulcers are either single or multiple They seldom penetrate the muscular layer. Pyloric stenosis is secondary to either a tuberculous ulcer or a granuloma

Often the symptoms of tuberculosis of the stomach are obscured by the other symptoms of the disease In many cases gastric symptoms may be absent There may be peptic ulcer-like epigastric distress, and vomiting of a sufficient severity to suggest pyloric obstruction The loss of weight and strength is constant and severe When gastric tuberculosis is advanced, hemorrhages from the stomach often occur

On examination, palpation often reveals a gastric mass, but more frequently roentgenologic examination reveals signs of organic gastric disease. Clinical evidence of tuberculosis elsewhere in the body is usually present In most instances advanced tuberculosis of the lungs or of the intestinal tract is present.

The diagnosis of gastric tuberculosis cannot be made without confirmation by histologic study. The presence of tuberculosis in the lungs or elsewhere in the body, particularly if the disease is in an advanced stage, may suggest the possibility of gastric involvement with tuberculosis.

Hypertrophic gastritis and cancer do not have a cause-and-effect relationship When an aged patient gives a short history of epigastric distress after dietary indiscretions or after indulgence in alcoholic beverages, with or without having had an acute illness or hypertrophic gastritis, it is suggestive of cancer and not an exacerbation of a gastritis This history is more suggestive of cancer if there are nausea after meals, anorexia and regurgitation and vomiting. In these cases anemia may be present, often of a hypochromic iron deficiency type.

The diagnosis of hypertrophic gastritis which simulates cancer of the stomach is established by exclusion of cancer of the stomach by roentgenologic examination and endoscopic recognition of the gastritis

Atrophic Gastritis. Atrophic gastritis is characterized by a thinning of the mucous membrane and often of the rest of the coats of the stomach

Since this disease affects patients of middle life and later, at least one or more of the etiologic factors enumerated as possible causes of chronic gastritis have had time to act, and since no one can live a model life and never indulge in at least a cup of hot tea, a highball, or in pepper sauce on turnip greens, one or more of the irritants will have been ingested by the patient. An "etiologic agent" can always be found

The digestive symptoms in atrophic gastritis are of variable duration and usually of periodic occurrence The common complaint is a postprandial, localized, dull epigastric discomfort accompanied by anorexia and nausea. Night pain is not present and relief does not follow the ingestion of food and antacids. Vomiting and bleeding are rare General symptoms are perhaps the most definite There are recurrent episodes of extreme fatigue and weakness; these patients are sad, depressed, and often have been lifelong dyspeptics and in the habit of condemning themselves for having eaten or drunk the wrong things

EXAMINATION IN CHRONIC GASTRITIS. The physical examination of a patient who is suspected of having chronic gastritis is performed in order to eliminate some other abdominal or constitutional disorder capable of causing the complaints. If tenderness is present in the epigastrium or in the upper part of the abdomen, it is widespread and not extreme

In some there is present sore tongue or sore mouth Some patients experience numbness or tingling in the hands and feet In many cases the blood is normal or, on microscopic examination, may be slightly hypochromic The gastric secretory findings may include achlorhydria or a normal acidity

If the gastroscopist reports an acute or a catarrhal gastritis involving only the uppermost layers of the gastric mucosa, this finding should not be considered diagnostically conclusive, particularly if the process consists of only small areas of erosion attended with a minimal amount of adjacent inflammatory reaction This type of gastritis is evanescent and tends to disappear rapidly However, in some instances it may progress to the hypertrophic state or the mixed state

If the gastroscopist reports gastritis, the mucosa presenting a simple swelling and congestion of the gastric folds, which have lost their normal smooth glistening appearance, or some thickening of the gastric mucosa and the presence of mucopurulent secretion between the folds, the condition is usually hypertrophic gastritis If the condition should be more severe, mention will be made that the mucosa assumes a nodular or cobblestone appearance. If the disease is advanced, a distinct hypertrophy of the gastric rugae, patches of ulceration and surrounding edema, infiltration, and a loss in the normal elasticity of the gastric wall will be described This latter type of gastritis is recognized by the roentgenologist

Atrophic gastritis occurs less frequently than other forms of gastritis and is reported as being characterized by extreme thinning of the gastric mucosa The gastric rugae disappear and the submucosal vessels come into view. The mucous

swelling, necrosis, and erosion. Pyloric obstruction may enhance a mycotic infection

The symptoms in either mode of infection by any kind of fungi may simulate those of acute or chronic gastritis, ulcer, or malignant disease of the stomach.

The diagnosis is based on the laboratory findings and on biopsy performed at the time of surgical operation Heavy mold flora, revealed by examination of the vomitus or of the gastric contents, may suggest the diagnosis Fungi present in achlorhydric gastric contents have little or no significance.

The prognosis is guarded in cases of proved blastomycotic or actinomycotic invasion. The patients who have other mycotic infections seem to fare better.

Diseases of the Stomach Due to Foreign Bodies in the Stomach. Foreign bodies present in the stomach may be small bodies accidentally or intentionally swallowed, bezoars, and endogenous bodies such as gallstones.

Swallowed Foreign Bodies. The smaller solid objects accidentally or intentionally swallowed, such as seeds, fruit stones, pebbles, coins, marbles, buttons, pieces of bones, and finger rings, usually emerge from the anus without causing injury A sharp object such as a fish bone, an open safety pin, or a needle may pass on to the stomach or intestine and produce abrasions of the mucous membrane or penetrate more deeply to cause bleeding and later abscess formation, and occasionally granuloma. Actual perforation is rare, but walling off of the perforated object and the resulting formation of an abscess or a foreign body granuloma is relatively common A needle may migrate to distant parts, for instance, to the heart

Obstruction of the normal pylorus as the result of a swallowed foreign body may occur, but more often the obstructed pylorus is abnormally small Obstruction in the intestine, if such occurs, takes place most frequently in the lower part of the ileum or in the descending colon

If the patient has mental disease, the presence of gastric symptoms and of a palpable abdominal tumor requires consideration, in differential diagnosis, of the possibility that he has swallowed a foreign body The ingestion of pieces of soluble heavy metals rarely causes metallic poisoning In the mentally normal patient the history of swallowing a foreign body is obtained

Before the diagnosis of swallowing of an object is made, the examiner should try to be sure that a missing article has been swallowed, not lost Attempt at removal of the object, when first seen roentgenoscopically, requires judgment and experience There is no emergency great enough to justify the attempt at removal by an unqualified operator, for use of the gastroscope by unskilled hands may prove disastrous It is wise to watch and wait if the swallowed object is small and not sharp Frequent roentgenoscopic re-examinations will often reveal the satisfactory passage of the object through the alimentary canal If the swallowed body remains in the stomach, the decision concerning the type of treatment to be employed is made by the endoscopist, whose services should be obtained as soon as the emergency arises

The large objects swallowed by the performer at the circus and by the insane usually find their way out of the alimentary canal through the anus Large objects, however, such as spoons, knives or forks may cause traumatic ulceration, perforation, or obstruction in some part of the alimentary tube.

The Bezoars. The bezoar is a concretion in the stomach It may be composed of hair (trichobezoar), vegetable or plant fibers (phytobezoar), a combination of hair and vegetable fibers (trichophytobezoar), or mineral medicaments or any other insoluble substance of physical and chemical constitution which can withstand the action of the gastric juice and the emptying efforts made by the stomach

Trichobezoar or hairball is the type of bezoar most frequently observed in man. Hair swallowing is confined principally to nervous children and mentally deranged women A trichobezoar may fill the stomach, making a complete cast of the organ.

Syphilis of the Stomach. Gastric manifestations during the primary stage of syphilis are rare In more advanced syphilis, however, there may be present mild gastric dyspeptic symptoms such as anorexia, nausea and epigastric discomfort. These symptoms represent the local gastric response to a systemic infection.

Congenital syphilis of the stomach is not encountered in clinical practice of medicine. Acquired syphilis of the stomach is commoner in men than in women and occurs 10 to 15 years earlier than does carcinoma of the stomach

It is difficult to estimate the incidence of gastric syphilis O'Leary has recorded a clinical diagnosis of gastric syphilis a number of times. Many of O'Leary's patients were examined by Eusterman, who concurred in the diagnosis.

Many pathologists have studied the stomachs of syphilitic patients but have never made a diagnosis of gastric syphilis on histologic findings alone However, it seems that syphilis of the stomach can be manifested by (1) a single lesion, or multiple lesions, taking the form of a nodular ulcerative syphilid, (2) diffuse nodular infiltration or chronic fibrosis and (3) in some cases, multiple serpiginous ulcers

Eusterman found it impossible to formulate a definite symptomatology For the purpose of clinical analysis only, he divided cases of gastric syphilis into three groups, which in the following enumeration are described in order of frequency of occurrence. (1) Those in which the onset of symptoms of epigastric distress or pain occurs immediately after meals and there is a quantitative type of dyspepsia The symptoms become progressively worse and the patients eventually require frequent feedings—evidence of a reduced gastric capacity Vomiting and pain are definite, but nausea and anorexia are much less evident than in gastric carcinoma The patients are often in a state of partial or advanced starvation. (2) Those termed the ulcer type because of the "pain-food-ease" sequence The symptoms are not so definite as those that occur in duodenal ulcer (3) Those, the smallest group, in which symptoms begin with mild gastric discomfort, often occurring about one-half hour after meals Ingestion of food or alkali fails to give relief The discomfort increases and there is a tendency for the distress to appear earlier after meals. Gradually there is a loss of strength and weight.

The general examination may reveal evidence of pre-existing or present active syphilitic lesions

The diagnosis of gastric syphilis often is impossible Existence of the disease may be suspected, however, and at times the diagnosis is made if there are the following findings· (1) untreated tertiary syphilis, (2) defect in the stomach apparent on roentgenologic examination, (3) failure to relieve the symptoms by usual treatment for ulcer and (4) symptomatic relief with disappearance of the roentgenologic defect after appropriate antisyphilitic treatment

It is not often wise to try to prove a diagnosis as outlined In many cases the evidence strongly favors the diagnosis of carcinoma of the stomach In these cases surgical exploration should be advised.

The term catarrhal luetic gastritis when used, indicates gastritis and achlorhydria in a case of proved syphilis

Mycotic Infections (Including Actinomycosis) of the Stomach. Local circulatory disturbances in the gastric mucosa may predispose toward fungous disease of the stomach. A diphtheria-like membrane may be formed at first, to be followed by ulceration. The ulcers may be single or multiple, small or large. They rarely penetrate or perforate. The necrotic tissue from such lesions is infected with the mold The sulfur bodies of the ray fungus may be discovered in an actinomycotic ulcer.

During the course of an infection by any one of the higher plant organisms, and particularly in blastomycosis, the stomach may be infected by a *blood-borne infection* In a stomach affected by a blood-borne infection the capillaries of the gastric wall are obstructed by the organisms, with resultant hemorrhagic gastric

tion resulting from adhesions or constriction at the site of the sutured perforation. In rare instances hourglass deformities are associated with gastrojejunal ulceration, partial resection of the stomach and gastrostomy. In an occasional instance the deformity seems to be idiopathic in origin

In hourglass contraction due to gastric ulcer the communication between the upper and lower segments is situated near the lesser curvature, whereas in syphilis and cancer the communication often is in the middle of the stomach. Pyloric stenosis is found in 1 of every 4 stomachs which have hourglass deformities.

The patient often complains of having had recurring attacks of epigastric distress occurring after meals. The symptoms observed are those of gastric or duodenal ulcer. On palpation there may be epigastric tenderness In thin patients peristalsis may be visible

The clinical recognition of hourglass stomach is not possible The roentgenologic examination may reveal more than one contraction producing deformities Trilocular and multilocular stomachs may be described by the roentgenologist, and these have the same etiology and significance as the common hourglass deformity.

Tumors of the Stomach. New growths of the stomach comprise both benign and malignant tumors

Benign Tumors. In the experience of Eusterman only 1.3 per cent of all gastric tumors proved by operation were benign

The incidence of benign gastric tumors does not differ in the two sexes.

Benign gastric tumors are composed of epithelial, connective, vascular, nervous, fatty, or mixed tissues, or arise in association with these tissues Eusterman recorded distribution in order of the frequency of occurrence as follows (1) epithelial origin, adenomatous polyps, adenomas (benign cystic polyp), polyposis, and papillomas and (2) connective tissue origin leiomyomas, fibromyomas, adenomyomas, myxofibromas, hemangiomas, fibromas, neurofibromas, lipomas and dermoid cysts

SYMPTOMS The symptoms of benign tumors of the stomach depend on the size, location, and extension of the growths and on whether ulceration, bleeding, or malignant change is present The small tumors situated away from the sphincters, and even the large tumors in the fundus, do not cause subjective symptoms until they become large enough to be manifested on account of size A benign neoplasm situated near the esophageal orifice causes dysphagia When situated near the pylorus, there may be manifestations of obstruction of the pylorus

The duration of the symptoms attributed to benign gastric tumors varies between 6 and 18 months Massive hemorrhage into the stomach is the most constantly present symptom This is particularly true of leiomyoma, adenoma and neurogenic tumors There is a continuous loss of blood between severe hemorrhages or independently of them Anemia frequently is severe The association of gastric polyp with pernicious anemia and gastroscopic evidence of atrophic gastritis and carcinoma of the stomach occurs frequently enough to be considered a significant relationship

The prolapsing of a polyp through the pylorus may cause sudden acute severe [illegible] e stom- [illegible] polyps [illegible] pyloric obstruction

Benign tumors of the stomach may be multiple as in gastric polyposis A gastric polyposis may be present and symptomless if bleeding has not occurred. When there are symptoms, they are not distinctive If bleeding has occurred, there are often weakness and pallor These tumors are potentially malignant, but they may permit of reasonable health for a number of years

In the absence of pyloric obstruction or severe anemia the physical examination is important because of the negative findings. Palpable benign lesions of the stomach are rare, although large tumors may be palpated If an anemia is present,

The *phytobezoar* is composed primarily of vegetable matter from the ingestion of certain foods Enmeshed in its substance there are also food materials of other types and epithelial detritus Some of the causative ingredients that have been observed in phytobezoars are celery, the skins and seeds of prunes, plums and muscadines, and cotton. In about three fourths of all cases, however, the chief offender is the fruit of the wild persimmon Persimmons contain a considerable amount of pectin and a high percentage of the soluble "shibouî" gum, which is an effective mordant in the formation of phytobezoars.

Trichophytobezoars are composed of both hair and vegetable matter. Formation of the foreign body may follow the drinking of furniture polish, which is an alcoholic solution of shellac and resins The shellac and resins are precipitated in the stomach after the drinking of water

Various medicaments have been retained in the stomach as foreign bodies

The offending substance or substances may be eaten on one occasion or on several occasions without immediate symptoms Months or even years may elapse before manifestations appear The symptoms present depend on the size of the bezoar Frequently the symptoms comprise a sense of dragging, fullness, lump or heaviness in the epigastrium, cramplike epigastric pain and periodic attacks of vomiting. As time passes, gastritis develops as a result of the foreign body, and the symptoms are those of gastritis As the bezoar increases in size, symptoms of pyloric obstruction appear Peptic ulcer may develop concomitantly with the bezoar, and with its advent the characteristic symptoms of peptic ulcer disease are present An epigastric tumor may be palpated

The roentgenologic diagnosis of bezoar usually is definite. When there is a history of the swallowing of hair or persimmons or other significant material, and there is present a freely movable, palpable tumor in the epigastrium, the tentative diagnosis of bezoar is justified

Endogenous Foreign Bodies. Gallstones occasionally gain entrance into the stomach through a fistula, cholecystogastric or cholecystoduodenal The stone may be vomited, but usually it passes into the intestine and if it proceeds beyond the lower part of the ileum, will be expelled through the rectum

In some cases foreign bodies enter the stomach as a result of violence

A foreign body which would pass through the normal pylorus may be retained in the stomach as a result of pyloric stenosis In the stomach of a patient who has pyloric stenosis the surgeon may find seeds, fruit skins and masses of food detritus which cannot pass out. In some instances antacid tablets of magnesium carbonate, calcium carbonate and similar drugs may be found by the surgeon or revealed by roentgenoscopic examination

Diseases of the Stomach Due to or Consisting of Static Mechanical Abnormality. *Prolapse of the Gastric Mucosa Through the Pylorus.* Prolapse of the gastric mucosa through the pylorus is a rare cause of gastric symptoms

Moderate redundancy of the pyloric mucosa is common, and is without symptoms When the prolapsing mass is large, there are gastric retention and partial pyloric obstruction When complete prolapse into the duodenum occurs, the differentiation between pedunculated tumor and prolapsing gastric mucosa will often be impossible before surgical operation is performed If roentgenologic examination reveals a large defect in the pyloric canal and a negative shadow in the duodenal bulb, the condition may be diagnosed correctly by the roentgenologist However, often it may be impossible to distinguish it from pyloric ulcer, hypertrophic gastritis, or carcinoma

Organic Hourglass Deformity of the Stomach. In an hourglass deformity of the stomach the viscus is divided into two cavities connected by a channel This contraction occurs more frequently in women than in men The usual cause is a healed peptic ulcer which was or is situated in the middle segment of the stomach. However, an hourglass deformity of the stomach may develop after a free perfora-

tion resulting from adhesions or constriction at the site of the sutured perforation. In rare instances hourglass deformities are associated with gastrojejunal ulceration, partial resection of the stomach and gastrostomy. In an occasional instance the deformity seems to be idiopathic in origin.

In hourglass contraction due to gastric ulcer the communication between the upper and lower segments is situated near the lesser curvature, whereas in syphilis and cancer the communication often is in the middle of the stomach Pyloric stenosis is found in 1 of every 4 stomachs which have hourglass deformities

The patient often complains of having had recurring attacks of epigastric distress occurring after meals The symptoms observed are those of gastric or duodenal ulcer *On palpation there may be epigastric tenderness. In thin patients peristalsis* may be visible

The clinical recognition of hourglass stomach is not possible. The roentgenologic examination may reveal more than one contraction producing deformities Trilocular and multilocular stomachs may be described by the roentgenologist, and these have the same etiology and significance as the common hourglass deformity.

Tumors of the Stomach. New growths of the stomach comprise both benign and malignant tumors

Benign Tumors. In the experience of Eusterman only 1.3 per cent of all gastric tumors proved by operation were benign

The incidence of benign gastric tumors does not differ in the two sexes.

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The prolapsing of a polyp through the pylorus may cause sudden acute severe symptoms of pyloric obstruction Retraction of the prolapsed polyp into the stomach usually occurs and is followed by symptomatic relief Prolapsing pyloric polyps often bleed so that anemia may accompany the syndrome of intermittent pyloric obstruction

Benign tumors of the stomach may be multiple as in gastric polyposis A gastric polyposis may be present and symptomless if bleeding has not occurred When there are symptoms, they are not distinctive. If bleeding has occurred, there are often weakness and pallor. These tumors are potentially malignant, but they may permit of reasonable health for a number of years

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his contention that there is a parallelism between the degree of differentiation of the cells, the duration of life and the number of successful resections in the carcinomas. The prognosis varies proportionately; cancers of grade 1 are the most susceptible to resection and those of grade 4 the least favorable. However, there are notable exceptions to this rule.

Approximately one half of all gastric cancers occur in the pyloric segment and in the adjacent antrum The order of occurrence, excluding the pylorus, is the lesser curvature, the cardial end of the stomach, and the anterior and posterior walls of the body of the stomach.

The involvement of the nodes above the inner end of the left clavicle (Virchow) and in the left axilla is a demonstration of distant lymphatic permeation metastasis in carcinoma of the stomach. The thoracic duct drains the abdomen and receives tributaries from nodes in the left side of the thorax, whereas the right lymphatic duct has no direct communication with the stomach Therefore metastasis is usually limited to the left side.

Metastasis to the liver arises from lymphatic permeation along the portal vein and by the portal blood stream A sudden and diffuse enlargement of the liver by numerous nodules is probably of portal vein origin Cancerous infiltration of the lymphatics of the round ligament of the liver leads to superficial umbilical metastasis

When blood-stream embolism occurs, the lungs are often involved. Metastasis may occur also in the bones, kidneys, brain and meninges, liver, spleen and skin. Small nodules in the skin are rare and when present are late in the course of carcinoma and are a sign of widespread metastasis

Distant metastatic lesions within the abdomen causing peritoneal carcinomatosis may occur in cancer of the stomach An example of such transplantation is the palpable nodes in the rectal shelf in cases of carcinoma of the stomach

Occasionally gastric symptoms suggesting intrinsic malignant disease are due to *secondary invasion* of the stomach from a primary lesion in an adjacent organ. Lesions of the pancreas and the transverse colon are the commonest offenders

Gastric carcinoma affects all of mankind, white, yellow, red and black, savage and civilized Gastric carcinoma is rarely present in persons less than 30 years of age. Approximately three fourths of all patients who have this disease are more than 50 years old Cancer of the stomach occurs in two men for each woman so afflicted

Generally it is a safe practice to tell the patient that, in so far as is known, cancer of the stomach is not due to anything that he ever did or to anything that has been done to him

Symptoms The constitutional symptoms of gastric carcinoma are frequent early symptoms Loss of body weight, a sensation of increasing fatigue, lack of endurance or the inability to carry on the ordinary day's work may be felt before any dyspeptic phenomena occur These symptoms may or may not be accompanied by pallor Pallor in other instances may be the only reason why the patient visits the physician Occasionally, only loss of body weight is the reason for his seeking help

The number of instances of inoperable carcinoma of the stomach discovered annually among physicians, nurses and other members of the staffs of hospitals, clinics and medical schools indicates that early recognizable symptoms of gastric carcinoma are not known If the difficulty of early diagnosis of the disease were realized by physicians generally, there would be less criticism of the physician "elsewhere" for not making the diagnosis. The duration of symptoms before the patient consults a physician is usually about 6 months This duration of symptoms is estimated after manifest carcinoma is present.

In many instances of carcinoma of the stomach there are no symptoms, before metastatic lesions are discovered, that signify its presence to the physician or that indicate to the patient that all is not well In the tense person in whom a cancer of the stomach has been accidentally discovered, the history of symptoms obtained

it is often of the macrocytic type. Gastroscopic examination may be of some diagnostic value in the differential diagnosis of intragastric tumors, particularly in the differentiation between true polyposis and pseudopolyposis associated with hypertrophic gastritis

Roentgenologic and occasionally endoscopic examinations are essential to the making of a clinical diagnosis of tumor of the stomach Determination of whether or not the tumor is benign depends on histologic study after the tumor or a specimen of the tumor has been removed.

Malignant Tumors. *Carcinoma of the Stomach.* The cause of carcinoma of the stomach, like that of all other carcinomas, is unknown. The theories of the origin of gastric carcinoma embrace heredity, the irritative agents of food and drink, and the precancerous lesions

Occasionally carcinoma of the stomach occurs in several members of a family. Such familial incidence of the disease has directed attention toward heredity as a factor in its pathogenesis Carcinoma has been recorded in identical, or unioval twins. The simultaneous occurrence of a similar symmetric tumor in each of a pair of homologous (unioval) twins tends to establish a basis for assigning a genetic factor to some of these tumors Often susceptibility to cancer behaves like a recessive characteristic, and insusceptibility like a dominant characteristic

In a desire to help patients and to cure cancer of the stomach it is necessary to consider as causes of cancer of the stomach certain precancerous lesions Lesions that may precede the development of gastric cancer, particularly in middle-aged patients, are gastric ulcer, gastritis and benign tumors. It must be known, however, that there are no objective data to prove that gastric cancers are related etiologically to chronic gastritis The rarity of gastritis complicated by polypoid hyperplastic changes precludes the assumption that this condition is an important predisposing lesion of gastric malignant disease It is known, however, that some benign gastric tumors, such as leiomyoma and neurilemmoma, undergo malignant change. Gastritis is often associated with pernicious anemia Also there is present a greater susceptibility toward the development of gastric carcinoma in those who have pernicious anemia and in members of their families than in those who do not have pernicious anemia

DEFINITIONS The following types of carcinoma are described by the pathologist. simple adenocarcinoma, papillary carcinoma, colloid or gelatinous carcinoma, medullary carcinoma, and scirrhous carcinoma

Simple adenocarcinoma is intimately associated with the gastric tubules Extension of the growth often reaches the greater and lesser omenta and neighboring viscera and may invade them Metastasis to the regional lymph nodes and the liver ensues.

The term papillary is often applied to carcinoma arising in a polyp. Usually a tumor of this type is accorded a good prognosis after radical resection, since invasion of the gastric wall is rather slow and metastasis is comparatively late If metastasis occurs, it is to regional lymph nodes and the liver

The colloid or gelatinous carcinoma is an adenocarcinoma in structure, characterized by a preponderance of the mucus-producing cells, which rapidly infiltrate the muscular layer, frequently metastasizing to the regional lymph nodes and to the liver.

In the medullary type cells preponderate, connective tissue is scarce. The medullary adenocarcinoma may be diffuse and infiltrative rather than circumscribed and ulcerating Early invasion of the lymph nodes and widespread metastasis occur

The scirrhous carcinomas are of two forms, the circumscribed and the diffuse. The circumscribed type may simulate ulcer in its gross appearance

The diffuse scirrhous carcinoma often produces a shrinkage of the stomach into a rigid hollow structure, the leather bottle stomach or linitis plastica When this tumor invades the walls of the stomach they lose their pliability

Broders, believing that the extent of differentiation of the cells in the growth might prove of value in prognosis, graded malignant tumors on a basis of 1 to 4, grade 1 being the least malignant, and grade 4 the most malignant. He has many data to support

above the inner aspect of the left clavicle is present; this is often significant of cancer of the stomach However, this node may be enlarged in cancer of the urogenital tract or the mediastinum, in lymphoblastoma and, occasionally, in infectious mononucleosis, tuberculosis or syphilis. Likewise a firm enlargement of nodes beneath the lateral edge of the pectoralis major muscle or deeper in the axilla, in the absence of a similar node on the right side or of disease of the breast, may be a significant finding but in itself of little diagnostic importance. Occasionally fixation or induration of the umbilicus is observed Of the findings on physical examination that are indicative of abdominal carcinomatosis, a hard, firm, usually irregular mass palpated above the prostate gland or in a comparable position in the female is the most important This finding alone is only a diagnostic suggestion, since retroperitoneal lymphosarcoma and extension from ovarian malignant disease produce a similar hard mass in the cul-de-sac.

Analysis of gastric contents in the determination of the residuum in the stomach of a fasting person is of diagnostic importance in the presence of gastric carcinoma with pyloric obstruction. The amount of residual gastric contents may be 500 ml or even 1,000 ml or more

In 3 of every 4 instances of gastric carcinoma the ordinary analysis of the functional gastric contents reveals the degree of gastric acidity to be either achlorhydria or a definite hypochlorhydria If the roentgenoscopic study reveals an ulcer deformity, the presence of achlorhydria confirms the diagnosis of carcinoma Peptic ulcer, for practical purposes, does not exist when there is no free hydrochloric acid in the gastric contents

The presence of anemia in cancer of the stomach is variable. Before the disease has progressed to involve much of the stomach or in instances when blood loss has been of a minimal degree, there may be no anemia In an occasional patient, a macrocytic anemia may be the outstanding feature of cancer of the stomach There is evidence to indicate that polyposis and cancer of the stomach are commoner in men who have pernicious anemia than in those who do not have it Severe and progressive microcytic anemia is always a feature of advanced cancer of the stomach

Diagnosis The diagnosis of carcinoma of the stomach is made by roentgenologic examination If the first examination does not yield positive findings, a second is performed If a carcinoma near the cardia is suspected, an endoscopic examination is made

The accidental discovery of a lesion during periodic health examination or at the time of a diagnostic checkup for a previous benign lesion, such as gastric or duodenal ulcer, or the finding of the cancer at the time of operation for some other condition seems to carry no better prognostic import than those found during investigations for them Cancer thus discovered may not have been found early, and it may not be resectable Fortunately some gastric cancers are resectable and curable when the patient first realizes by some means that all is not well and that an examination is needed, and when the physician consulted immediately has a roentgenologic examination of the stomach performed by a competent roentgenologist

In regard to the course and the prognosis of cancer of the stomach during the ensuing five years after the diagnosis is made, Berkson, Walters, Gray and Priestley have analyzed their losses as shown in the diagram (Fig 13-5).

Of the total number of 100 patients diagnosed to have gastric carcinoma 14 were living at the end of 5 years Of the 86 who were not living at the end of 5 years, the lesions of 20 had been judged inoperable on examination roentgenologically and physically Thirty-six more at the time of laparotomy had been found to have nonresectable lesions. Four died in the hospital after surgical operations had been performed Twenty-six died during the 5 years following operation

in retrospect is not of diagnostic value. From such a patient it is impossible to determine the duration of symptoms before a physician was consulted. Of the nature of the symptoms which are indicative of carcinoma of the stomach it is singularly true that the gastric symptoms are new. They have never been experienced previously. They are of short duration.

The presence of local symptoms directs attention to the stomach. Often there is mild epigastric discomfort which is a feeling of fullness after a moderate meal, or there is a light cramp after dietary indiscretion Belching may be a new experience to these patients The patients usually are relieved of these discomforts by reducing the size of the meals and getting more rest. These symptoms are not considered serious because they are commonplace experiences of many middle-aged persons who do not have cancer of the stomach In those who have the disease, a distaste or dislike for certain foods, particularly meats, is a definite symptom As the disease progresses, an annoying nausea replaces this symptom, and loss of weight and weakness ensue

The nausea may be relieved by regurgitation or vomiting of small amounts of food after dietary indiscretions or after the eating of large meals. Vomiting may supersede the nausea and thus be the symptom for which relief is sought In the beginning, vomiting may occur only occasionally, the intervals between the episodes of vomiting are symptom free

In some instances of carcinoma of the stomach the illness begins with postprandial distress, which is relieved temporarily by antacids and food The patient may have taken a vacation, in the course of which these symptoms were relieved if the diet was restricted Some patients, without apparent provocation, experience gross bleeding before other local or constitutional symptoms have occurred In the presence of cancer at the cardial end of the stomach, substernal oppression, mild dysphagia, or cough may occur after the taking of food or liquids

Patients who have had dyspeptic symptoms for many years may or may not have had a change in such symptoms, an occurrence often narrated as a sure indication of early cancer These symptoms are changeable without the presence of a carcinoma

A patient may discover a lump in the epigastrium as the first symptom Large tumors in the body of the stomach may not cause local symptoms

A few patients who have gastric carcinoma are aware first of swelling of the abdomen due to ascites Backache or pathologic fractures from a metastatic lesion of the spinal column may instigate a series of roentgenologic investigations which result in the discovery of a carcinoma in the stomach

Symptoms due to a metastatic pulmonary lesion, especially of the left lung, may be of primary significance In rare instances there may be pleurisy or consolidation of this lung without any gastric symptoms though a cancer of the stomach is present and far advanced

The symptoms of pulmonary hypertension from carcinomatosis of the lung which is secondary to a primary growth in the stomach may be difficult to associate with gastric disease

Despite vicissitudes of the symptoms in early cancer of the stomach, no physician can long live at peace with his own conscience who treats a middle-aged or aging patient for any new ailment of the stomach for more than one or two weeks without a roentgenologic examination If the roentgenologist reports negative results, the examination should be repeated if symptoms persist.

Examination. Visible peristalsis occasionally occurs in early gastric carcinoma which is present at the pylorus. Epigastric tenderness is rarely found alone. A *palpable mass* varies with the somatic type of the patient, the thickness of the abdominal wall, and the site and the size of the tumor. The liver may not be enlarged or it may be irregular, firm and enlarged In an occasional instance a firm node

Diagnosis of gastric sarcoma without resort to surgical exploration and biopsy is not possible

Among patients afflicted with sarcoma, the greatest number who survive 5 years are those who have lymphosarcoma or Hodgkin's disease.

Lymphogranulomatosis and Malignant Lymphadenoma (Hodgkin's Disease) of the Stomach. The lesions of lymphoblastoma of the stomach may be situated on the lesser curvature at the cardial end and extend into the esophagus, or may involve a greater part of the stomach.

The symptoms are those of gastric malignant disease. The constitutional symptoms of Hodgkin's disease may be added Occasionally the symptoms and signs common to the abdominal type of Hodgkin's disease, such as recurring fever, diarrhea, pruritus ani et vulvae, jaundice, and ascites are present

A mass may be palpable Splenomegaly is often present when there is gastric involvement The liver is less often enlarged than the spleen. Superficial lymph nodes may be enlarged. Anemia, leukopenia, and an increase in the number of transitional cells, eosinophils, and blood platelets may be found. The roentgenologic features are not characteristic.

The diagnosis of Hodgkin's disease of the stomach is established by histologic examination If Hodgkin's disease has been diagnosed by means of biopsy of a lymph node in a patient who gives roentgenologic and gastroscopic evidence of an infiltrating lesion in the gastric wall, malignant lymphadenoma of the stomach is likely.

Linitis Plastica This condition is called also leather bottle stomach, cirrhosis of the stomach, gastritis, and granulomatosis fibroplastica, hypertrophic gastritis, gastric sclerosis, Brinton's disease, cirrhotic gastritis, and fibromatosis ventriculi

In the great majority of cases of linitis plastica the gastric disease is malignant. In a few instances linitis plastica is produced by benign affections

The gross appearance of the stomach in linitis plastica is that of a rigid, hollow viscus The walls are several times their normal thickness When the stomach is cut with a knife, it is observed to be hard The mucosa is wrinkled, nodular and uneven The peritoneum over the lesion is opaque and pearly white

The disease occurs oftenest in men from 40 to 70 years of age Women less frequently have the disease These men and women often have, in addition to their stomach trouble, cardiovascular disease, addiction to alcohol, or infection with syphilis or tuberculosis

A sensation of surfeit follows even small meals Later, postprandial fullness, belching, regurgitation and vomiting occcur Anorexia and sitophobia soon appear, and the constitutional symptoms of loss of weight, undernutrition and anemia ensue. A palpable mass in the epigastrium is present in three fourths of the patients Anemia and cachexia are common Analysis of gastric contents often reveals achlorhydria

The preoperative diagnosis of linitis plastica is based on roentgenologic study

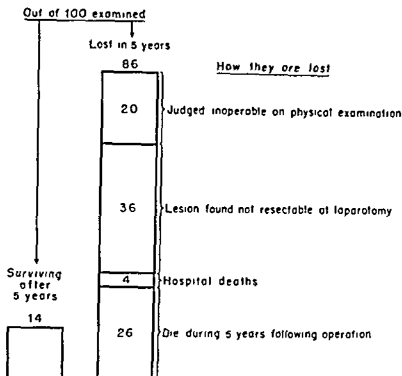
The outlook for permanent cure after gastrectomy is uncertain, but life may be prolonged even if carcinoma is responsible for the condition If the disease is due to inflammatory processes in an individual case, a cure by gastrectomy may be obtained without the likelihood of recurrence or metastasis

PEPTIC ULCER

A peptic ulcer results from dissolution of a small region of the mucous membrane and often of the deeper coats of the stomach or the duodenum which are regularly exposed to gastric secretions

Etiology The etiologic factors of peptic ulcer which have been postulated are worthy of enumeration only because each has had serious protagonists. There are the hypothesis accusing intragastric factors as being responsible, and those accusing extragastric factors as being responsible.

In all of the various studies on series of patients who have cancer of the stomach, it is definitely revealed that the best results are obtained from resection of the stomach when metastasis has not occurred The results from surgical treatment



From Berkson J, Walters, W, Gray, H K and Priestley J T, Proc Staff Meet Mayo Clin 27 137 1952

Fig 13-5 Analysis of 5-year losses from cancer of the stomach

are not good However, surgical treatment is the only available curative procedure despite its limitations.

Sarcoma of the Stomach In only 1 per cent of the reported cases of tumors of the stomach are the growths sarcomas (Ewing) The average age at which sarcoma occurs is between 45 and 50 years, approximately 10 years less than that for gastric carcinoma

PATHOLOGY Benign connective tissue tumors are often considered to be precursors of sarcomas, particularly neurilemmomas, leiomyomas and fibromas Neurofibromas associated with Recklinghausen's disease may undergo sarcomatous change. Hodgkin's disease of the stomach may not be suspected until biopsy studies have been made.

Metastatic extension of neurogenic sarcoma, lymphosarcoma and fibrosarcoma occurs late, if at all. Myosarcomas grow rapidly and metastasize comparatively early. Blood-borne metastasis often occurs in the more malignant types of sarcoma Round cell sarcomas and endotheliomas frequently invade the blood stream Enlargement of superficial lymph nodes may occur in association with gastric lymphosarcoma, and the differential diagnosis between Hodgkin's disease, leukemia, tuberculosis and lymphosarcoma may be difficult.

Massive bleeding is the commonest complaint among patients who have leiomyosarcoma. It may occur in conjunction with other types of sarcoma after the development of necrosis and ulceration Anemia, loss of weight and strength and other constitutional symptoms occur with about the same frequency as in carcinoma of the stomach.

pancreas distort the shape of the gastric wall on healing The greatest distortion is observed when an hourglass deformity of the stomach is formed.

Although ulcers situated in the *duodenum* heal well, they usually leave some deformity, but often of minimal degree It seems that in an occasional duodenal ulcer there may be associated with the healing process a diverticulum, the so-called ulcer-diverticulum. The diverticulum is usually single, but occasionally one will develop on each curvature

Free perforation of peptic ulcer occurs most frequently from ulcers situated on the anterior wall of either the stomach or the duodenum Ulcers of the posterior wall perforate just as frequently, but into the lesser peritoneal cavity, and they often are walled off by contiguous structures which prevent free perforation.

Occult bleeding of a peptic ulcer occurs from erosion into a very small vessel or from inflammation of recently formed granulation tissue. The amount of bleeding from a peptic ulcer does not always depend on whether the blood comes from granulation tissue or from a blood vessel

SYMPTOMS Pain is the first and the only symptom of uncomplicated peptic ulcer.

The pain in peptic ulcer is originated by peristalsis, local spasm, congestion, edema and inflammatory reaction about the ulcer and not by hunger. Edema has rendered the insensitive mucosa sensitive to pain Perhaps these reactions and the situation of the ulcer are more important than the degrees of acidity present.

In gastric ulcer, after food is taken, comfort occurs, lasting from one-half to one and a half hours, followed by pain which disappears when the stomach no longer contains food In duodenal ulcer from 2 to 4 hours of comparative comfort elapse after eating; then pain appears and remains until food again is eaten or until mealtime is passed

Pain from duodenal ulcer often comes in the late evening The most characteristic time of occurrence is between midnight and 3 00 A M The patient is awakened from sleep by pain which may continue for an hour or so unless milk, warm water, or antacid is taken In many cases of duodenal ulcer no pain of consequence occurs at any other time during the entire period of ulcer activity except that coming after midnight Pain situated in the epigastrium, after midnight, which awakens the patient from sound sleep is nearly always pathognomonic of duodenal ulcer

In duodenal ulcer symptoms may commence with an attack of severe epigastric pain extending to the right costal margin or to the back Such attacks may be repeated over a period of several years before the usual symptoms of duodenal ulcer are established A rare manifestation of duodenal ulcer has been described by Eusterman as pseudotabetic crisis, in which the symptoms cannot be distinguished from the gastric crisis of tabes dorsalis Without warning, severe epigastric pain of wide radiation occurs, associated with persistent vomiting This syndrome is most often present in hypersensitive patients and comes on when they are emotionally upset In such instances it may be difficult to determine whether or not a perforation of the ulcer has occurred

During the time that a duodenal ulcer is symptomless, there may be an exacerbation of pain just for one day or one night, the interval preceding and following such exacerbation being one of pain or epigastric soreness

The syndrome of peptic ulcer is characterized by the tendency for the pain to recur *periodically* during a particular phase of the digestive cycle daily for weeks, to be followed by periods of remission of all symptoms Episodes of peptic ulcer activity are usually self-limited, regardless of treatment. Patients often give a history of daily discomfort, lasting from 3 to 6 weeks, occurring during the spring or fall months, with freedom from pain during the summer and winter seasons. Seasonal recurrences are not so often present in those who have gastric ulcer as in those who have duodenal ulcer.

Fatigue, alcoholic beverages, excessive smoking, nervous tension, exposure to

The *intragastric factors* which have been held responsible are (1) disturbances attributed to tissue-destroying and tissue-resisting influences, (2) devitalization of circumscribed areas of tissue, (3) hydrochloric acid pepsin factor, (4) lack of mucous secretion, (5) internal trauma, (6) gastritis and (7) vascular factor.

The *extragastric factors* are (1) heredity, (2) infection (focal), (3) syphilis, (4) duodenal factors, (5) nutritional deficiency, (6) burns, (7) endocrine glands, (8) allergy, (9) brain and autonomic nervous system and (10) psychosomatic relationship. These are very important.

There has never been any doubt of the preponderance of duodenal ulcer in men since the beginning of extensive gastric surgery by W. J Mayo and C H Mayo The ratio is approximately 4 men to 1 woman

The average age of the patients at the time of commencement of duodenal ulcer is between 30 and 35 years, and at onset of gastric ulcer about 40 years Peptic ulcers may occur in the newborn, in children, and during growth and early adult life.

Gastric ulcers are of a larger average size (0 5 to 4 cm.) than duodenal ulcers, which usually are about 0 5 cm in diameter Malignant gastric ulcers are usually larger (1 cm or more in diameter) than benign gastric ulcers. The size of the lesion alone cannot be used to make the differentiation between a benign ulceration and a malignant one

Gastric ulcers are often situated on the posterior wall near the lesser curvature. An occasional, usually a large, gastric ulcer is situated in the cardial zone of the stomach, near the lesser curvature Prepyloric ulcers occur A prepyloric ulcer in an aging patient is suggestive of carcinoma *Duodenal ulcers* most frequently are situated within 1½ inches (3.8 cm.) of the pyloric ring on either the anterior or [illegible] more distal segments of the duodenum.

Peptic ulcer is usually a single lesion However, two, three or more chronic gastric ulcers may be present. The gastroscopist often finds one or more smaller ulcers in association with a large chronic ulcer In about 1 of every 10 patients who have gastric ulcer a second ulcer or an ulcer deformity will be found in the duodenum. Multiple duodenal ulcers can be demonstrated in 1 of every 4 patients who have duodenal ulcer Double ulcers may occur in opposition, one situated on the anterior wall and the other on the posterior wall ("kissing ulcers")

Regularly and characteristically peptic ulcers tend to recur after complete healing has taken place. Strangely, one of two healed scars in the stomach, or one of two scars, one in the stomach and the other in the duodenum, may become reactivated while the other remains healed

PATHOLOGY Peptic ulcers occurring in either the stomach or the duodenum are classified as acute or chronic

The *acute peptic ulcers* are distinguished from erosions on the basis of depth If the erosion penetrates deeper than the muscularis mucosae, the designation acute ulcer is correct. Erosions usually are limited to the ulcer-bearing region They may be found in association with active gastric ulcer, superficial gastritis, and hypertrophic gastritis or just alone.

A *chronic peptic ulcer* is a small excavated lesion involving one or more layers of the gastric or the duodenal wall The base and wall of the ulcer are covered by mucus, fibrin and necrotic material adjacent to a fibrotic matrix which separates it from the serosa and adjacent tissues. The amount and extent of the edema present vary with the degree of activity of the ulcer

The chronic ulcers have a tendency to heal Pathologists in their examinations find an equal number of healed ulcer scars and active ulcers.

Ulcers of the *stomach* often heal without leaving visible scars and without visible deformity of the gastric wall. Often however a visible fibrotic scar remains after healing. Ulcers situated on the posterior wall of the stomach which have perforated against the

discovered by applying pressure elsewhere in the abdomen or even over the tibiae Two types of epigastric tenderness during activity of peptic ulcer have been described (1) circumscribed superficial epigastric tenderness and (2) deep tenderness The differentiation of these is of little practical value. That there is, or is not, tenderness is as far as this sign need be pursued

Genuine muscle guarding indicates serosal irritation and is observed in cases in which ulcers have deeply penetrated the wall of the viscus or have subacutely perforated it. Absolute muscular rigidity is observed only when there is free perforation with inflammation and irritation of the anterior parietal peritoneum. In such cases rebound tenderness is to be anticipated

Peristalsis may be visible in the presence of pyloric obstruction. If peristaltic movements are not visible, an exquisitely tender abdomen should not be struck to elicit them

A study of the volume of *gastric secretion* and perhaps of the *acidity* is of value in obtaining information concerning the emptying of the stomach. In clinical practice achlorhydria is not encountered in peptic ulcer A patient suspected of having a peptic ulcer should not be given histamine.

DIAGNOSIS OF PEPTIC ULCER. *Gastric Ulcer* The clinical diagnosis of peptic ulcer of the stomach from the history and the physical examination is a presumptive diagnosis A more precise diagnosis is made by the roentgenologist, who may enumerate a number of defects of the stomach which has or has had an ulcer, in addition to the ulcer itself. The terms are self-explanatory (1) organic hourglass stomach, (2) shortening and stiffening of the lesser curvature, (3) perigastric adhesions

If the symptoms are suggestive of disease within the stomach and results of roentgenologic study are negative, gastroscopic examination may be of assistance. The gastroscope may demonstrate a gastritis not revealed by roentgenoscopic examination, and may help in the differential diagnosis of benign and malignant ulcerations.

Often malignant gastric ulcers are present in cases in which there have been no ulcer symptoms Metastasis may be found by physical examination The process is evidenced by an enlarged liver, and by metastatic extension to the rectal shelf (rectovesical pouch) and supraclavicular lymph nodes In many instances an endoscopic examination is necessary for diagnosis of a malignant lesion

A gastric ulcer in a patient of 40 years of age or more is suspected of being malignant Often the roentgenologist cannot say that the ulcer is either benign or malignant.

The first help diagnostically comes from the history If there has been epigastric distress, related to the digestive cycle, extending over many years, the gastric lesion is often benign, whereas if there is a history of only recent distress, more of fullness, soreness, or aching than of a gnawing discomfort, rhythmic or constant in character, the ulcer is often malignant An added factor supporting the possibility of malignancy is a distaste for food, leading to loss of appetite There will be loss of weight in those who cannot eat

Achlorhydria, demonstrated by the ordinary fractional analysis of gastric contents, eliminates the presence of a benign peptic ulcer. If there is ample hydrochloric acid present in the gastric contents and if the niche is of the deeply penetrating type on the lesser curvature, a trial of medical therapy may be justified for diagnostic purposes If at the end of 2 or 3 weeks there is no change in the size of the niche, the lesion should be considered malignant and surgical intervention advised.

Duodenal Ulcer The history and physical examination are sufficient for presumptive diagnosis of duodenal ulcer. As in gastric ulcer, the roentgenoscopic examination is the most precise diagnostic procedure There are duodenal ulcers, however, which cannot be diagnosed by roentgenologic methods. This statement is

excessive heat or cold, or unusual physical exertion may cause an *exacerbation* of ulcer symptoms or render ulcer pain more intense, and all tend to prolong the duration of ulcer activity However, at times of unusual demands on the ulcer patient, as occasioned by excessive grief, there may be temporary amelioration of symptoms for days or even weeks, to be followed by more severe symptoms when the nervous tension is lessened

The intensity of ulcer pain is related to (1) anatomic location of the ulcer, (2) its depth and (3) inflammatory reactions. Peptic ulcers in the body or middle section of the stomach cause less pain than ulcers situated near the cardia or the pylorus The severity of the pain is more nearly related to the depth of the ulcer than to its size, and is more definitely related to the extent of the inflammatory reaction surrounding the ulcer than to any other factor. An inflammatory reaction involving the serosa produces pain of great intensity. Serosal involvement is suspected when ulcer pain becomes constant during the day and is present during the digestive cycles before, during and after meals. However, a constancy of symptoms is present when there is an accompanying gastritis or duodenitis.

Rivers observed that a shallow gastric ulcer causes a poorly localized pain, whereas definite localization occurs in one half of all patients who have large gastric ulcers with subacute inflammation Most patients who have gastric ulcers of the perforating type have localization of pain in the left upper abdominal quadrant along the costal margin When a peptic ulcer invades the mesentery, mesocolon, or abdominal wall, the pain is referred to the thorax or the back. In perforating duodenal ulcer the pain is localized in the right upper abdominal quadrant Pain due to perforations of subacute ulcers situated on the posterior wall of the duodenum is referred through to corresponding levels of the back.

In the absence of epigastric discomfort in duodenal ulcer the pain may be situated near the midline of the back between the eighth and twelfth thoracic vertebrae. Pain here does not always indicate posterior perforation; in some cases, however, it may be looked on as an indication of a perforated ulcer of the posterior duodenal wall adherent to the pancreas Occasionally ulcer discomfort is present in the lower right abdominal quadrant and has the same characteristic rhythm as if situated in the epigastrium Peptic ulcer pain may be localized to the upper right quadrant without penetration of the ulcer against the liver, pancreas, lesser omentum, or gallbladder. Duodenal or gastric ulcer may be responsible for pain localized to the anterior part of the thorax, behind the sternum between the suprasternal notch and xiphoid

The characteristic features of the discomforts and pain of uncomplicated peptic ulcer may be summarized as follows· (1) rapid relief of pain after administration of soluble alkalies, (2) amelioration, by frequent feedings of milk, of all the discomfort produced by an ulcer and (3) palliative effect on ulcer pain by physical and mental rest, relaxation, the application of warmth to the abdomen, and use of mild sedatives.

Examination On physical examination of those who have uncomplicated chronic peptic ulcers there are no findings indicative of ulcer. The value of the [illegible] diseases which may be present. [illegible] ass directs attention at once to [illegible] ric symptoms The extent and localization of tenderness, if present, are delineated and evaluated

In acute peptic ulcer or chronic peptic ulcer during an acute exacerbation of symptoms a region of circumscribed tenderness at or near the midline of the epigastrium between the xiphoid cartilage and the umbilicus may be present. However, this is of little diagnostic value, for the asthenic patient will have tenderness in the midline of the epigastrium when pressure is applied over the aorta or the ventral surface of the vertebral column. In these cases similar regions of tenderness will be

symptoms The remaining 3 will have had known symptoms, often of short duration, suggestive of peptic ulcer.

SYMPTOMS. The pain is of abrupt onset. Intelligent patients may describe a feeling of a rapid spread of the fiery sensation in the epigastric region, often as if hot water were being poured into the upper part of the abdomen The extension and the severity of the pain vary. Often the pain is centered in the epigastrium and radiates to the whole middle of the body, including the back. References of pain from this section of the body are inconsequential. In an occasional patient the generalized pain subsides somewhat, or at least the pain becomes more severe in the lower part of the abdomen, often in the lower right abdominal quadrant There seems to be a collection of the extraluminal chyme in this part of the abdomen.

The patient assumes a position with thighs flexed upon the abdomen and resents any change of position Nausea and vomiting and the characteristic facies of agony and shock supervene. The skin is cold, and is covered by perspiration The respirations are panting and shallow. The temperature is subnormal. Death rarely occurs at this time If it does occur, it follows soon and is attributed to an overwhelming effect on the vasomotor centers.

From 1 to 4 hours after the perforation there may be a period of symptomatic improvement The pain may be less intense or largely disappear; the pulse, temperature and respirations approach the normal The patient, if not restrained, may desire to sit up or walk However, on attempting such movements the intensity of the pain may return

EXAMINATION The patient may be first examined during this period of quiescent symptoms However, if on examination of the abdomen boardlike rigidity is present, operation must be performed at once The pulse rate will soon increase and the temperature will rise, malar flush will develop, and the patient becomes apprehensive because a generalized peritonitis will be present

At no time after the perforation is there any relaxation of the abdominal musculature The rigidity may be present throughout the abdomen or it may be confined to the epigastrium, with muscle guarding of lesser degree in the lower part of the abdomen Like the pain, the rigidity may develop rapidly in the lower right portion of the abdomen because of the accumulation of the gastric contents there. On auscultation there is the silent abdomen of peritonitis On percussion the hepatic dullness may be supplanted by a tympanitic or resonant note. The absence of hepatic dullness, with the patient in the dorsal decubitus, is not, however, pathognomonic of [illegible]

Digital examination of the rectum may elicit tenderness when pressure is made toward the right cul-de-sac If a firm mass is palpated in the cul-de-sac in a patient of middle life, the perforation may have resulted from the rupture of an ulcerating gastric malignant lesion

One to 4 hours [illegible] it is 10,000 to 15,000 [illegible] philia The absence [illegible] tion In elderly patients and those whose resistance is lowered from any cause, leukocytosis may be absent In due time, if operation is not performed, the leukocytes increase in number and toxic manifestations are observed in them

The blood chemical findings are not disturbed until peritonitis and vomiting are established

proved by cases in which acute perforation *has developed after* repeated roentgenograms have been recorded as negative. The clinician, however, realizes that he is held responsible for *failure to diagnose* a peptic ulcer if it perforates, irrespective of negative results of roentgenologic examination.

There are patients who have epigastric distress identical with that observed in duodenal ulcer. *This distress may be* associated with excessive use of tobacco and alcohol or it may occur *in a member of the W.C.T.U.* Often these ulcer-like manifestations are due to functional digestive disorders as a part of a state of *nervous tension incident to vagotonia.* The analysis of gastric contents discloses hyperacidity and *hypersecretion. Roentgenologic* examination does not reveal abnormality.

The diagnosis *in these cases is recorded* variously as (1) pyloroduodenal irritability, (2) pseudo-ulcer syndrome, (3) irritable duodenum, (4) pyloric spasticity, and (5) "tobacco stomach."

and [illegible]

[illegible] about the daily affairs. These symptoms usually occur in the late *afternoon. Hypoglycemia* may be suspected but it is not usually [illegible]

[illegible] cases there is hypoglycemia. This hypoglycemia may be regarded as a concomitant rather than a primary factor in the production of some of these symptoms.

Occasionally in a man who has a duodenal ulcer, the blood count, subsequent to *a moderately* severe hemorrhage, will be only slightly below the normal level. After convalescence it may be discovered that the erythrocyte count is 6,000,000 or more *per cubic millimeter* of blood. Such an erythremia is of no diagnostic importance.

Differential Diagnosis of Peptic Ulcer. The difficulty in differential diagnosis is not that of finding the ulcer when it exists, but of ascertaining the cause of the ulcer-like symptoms in the absence of ulcer. If results of the roentgenoscopic examination are negative, the examination should be followed by a period of observation and then repeated. A definite diagnosis is not made unless results of roentgenologic or gastroscopic examinations are positive.

Perforation of Peptic Ulcer. Five of every 10 patients who have gastric or duodenal ulcer, who are treated adequately under a comprehensive regimen, will become symptomless. Of the remaining 5, 4 will have recurrence; if the patients are under treatment these recurrences will be inconsequential. The remaining patient will have symptoms which are intractable, and complications will develop which require surgical intervention, often death eventuates. This last, or the 1 patient, represents the group in which the more serious complications develop, and these complications often develop during the early part of an attack and often early in the course of the *disease. Perforation* is one of these serious symptoms and hemorrhage is the other. The patient who has perforation early in the course of the disease presents greater ulcer intractability and other complications than one who has had repeated recurrences unassociated with a serious complication.

Perforation by peptic ulcer is designated as acute, subacute and chronic.

Acute Perforation. In acute perforation there is a penetration through all of the coats often of the anterior wall of the viscus, and through this opening the intraluminal contents are poured into the peritoneal cavity. Death from peritonitis and toxemia generally occurs unless surgical closure of the perforation is made immediately.

Perforation into the lesser peritoneal cavity often occurs and is generally far less hazardous than perforation into the main peritoneal cavity. These posterior perforations are usually walled off immediately.

About 1 of every 4 who have perforation of peptic ulcer has not had ulcer

Hemorrhage from Peptic Ulcer. Hemorrhage from peptic ulcer, as well as hemorrhage from other gastrointestinal disorders, has been considered under the manifestations of digestive disease at the beginning of this chapter.

Recurring Peptic Ulcer After Surgical Operation. The course of a chronic peptic ulcer is characterized by remissions and relapses The usual relapse of peptic ulcer is just that much more disability and discomfort. After surgical operation if a relapse occurs it is a more serious matter.

The recurrence of ulcer symptoms after operation may be due to the following: The original ulcer has remained unhealed, and in such instances the symptoms are exactly as they were before the operation The site of the pain and tenderness is identical with that of the original ulcer The diagnosis of duodenal ulcer is favored by the roentgenologic demonstration of a functioning pylorus unless the original active ulcer has induced spasm and edema of the pylorus so that it is closed by these processes The differentiation between recurrent duodenal ulcer subsequent to gastroenterostomy and a small jejunal ulcer may be impossible except at the time of surgical operation Ulcers rarely recur after subtotal gastric resections

Gastrojejunal and Jejunal Ulcers. The incidence of gastrojejunal ulcer is difficult to determine. It may develop following any type of operation on the stomach in which the stomach has been anastomosed to the jejunum The surgical procedures consisting of subtotal gastric resection which remove the acid-producing mucosa have reduced the incidence of postoperative gastrojejunal ulcers

A gastrojejunal ulcer is a manifestation of a continuation of all the factors which are operative in the etiology of peptic ulcer There seems to be a peptic ulcer diathesis or a gastric diathesis in some patients who have peptic ulcer Gastrojejunal ulcer occurs most frequently in patients who mistakenly feel that surgical operation cures them They have persisted in use of tobacco and alcohol, have indulged their taste for foods at irregular hours, and have continued in a state of tension and fatigue. In addition to the foregoing causes, there are gastrojejunal ulcers due to faulty technic at the time of the operation

When the stomach is anastomosed to the ileum or to the colon, the symptoms simulate those of gastrocolic fistula diarrhea, fecal vomiting, fecal odor to the eructations, loss of weight and nutritional deficiency In an occasional individual so-called miserable good health may be present for many years. The symptoms may be those of an irritable colon syndrome

A *postoperative gastritis* as cause for symptoms in the anastomotic stomach should be made by exclusion In the absence of peptic ulcer and malfunctioning stoma the symptoms are due to postoperative gastritic changes if there is a sufficient degree of gastritis present on endoscopic examination to account for the symptoms

Finding of a *free perforation* is not common in gastrojejunal ulcer

A *subacute perforation* of either a jejunal or a marginal ulcer may penetrate to the serosa and become adherent to the transverse mesocolon, the colon, the omentum, or the anterior abdominal wall with or without formation of abscess or fistula. Often a walled-off perforation of this kind can be palpated as a tender indurated soft mass in the region of the stoma When such a mass is found, surgical operation is advised

SYMPTOMS There is usually an interval of freedom from ulcer symptoms of a few months to many years after the operation This symptom-free interval may be brief or absent in cases of acute anastomotic ulcer.

Gastrojejunal ulcer often causes symptoms not unlike those of the ulcer for which the operation was performed The discomfort appears earlier after the meal. Food and antacids fail to afford the same relief which they gave previous to the operation The relief is of shorter duration and the discomfort is often more severe.

The site of the discomfort changes It is lower, generally below the umbilicus. The radiation of the pain is over a wide area, often to the back, and sometimes upward into the left pectoral region The presence of peristaltic unrest and gaseous discomfort often mimics the irritable colon syndrome

Nausea and vomiting are common and these are symptoms that were not present

DIAGNOSIS The foregoing history and physical findings are unmistakable Pneu- ... patient has an acute

... be found at surgical exploration which cannot be differentiated clinically: (1) acute fulminating appendicitis with rupture, (2) acute intestinal obstruction and (3) acute pancreatitis.

In rare instances the following conditions cannot be differentiated: (1) biliary colic, (2) renal colic, (3) twisted pedicle of an ovarian cyst, (4) ruptured ectopic gestation, (5) ruptured diverticulum of the sigmoid colon, (6) mesenteric thrombosis and (7) Meckel's diverticulum.

One condition which may resemble that of a perforated ulcer is *arachnidism*, the bite of the black widow spider Arachnidism is associated with excruciating *abdominal pain, tenderness, rigidity*, and frequent nausea and vomiting. There is usually a history of the bite about the face or on the genitalia

In a number of patients who have tabes dorsalis a gastric crisis is the initial symptom If there is a history of ulcer, a proper diagnosis is impossible. The pathognomonic neurologic findings may be absent The gastric crisis begins with a very severe epigastric pain in association with tenderness and muscle guarding but not with a permanent rigidity of the abdominal muscles The one difference may be that in most cases of gastric crisis nausea and vomiting accompany the pain. These are usually absent in perforation of ulcer, particularly in perforated duodenal ulcer. Usually the patient suffering from ulcer perforation has had ulcer-like symptoms previously. The flat plate of the roentgenologic examination will not reveal pneumoperitoneum in gastric crisis Patients in crisis do not assume and maintain the immobile position characteristic of ulcer perforation and they frequently change their positions or may even walk the floor

Even if surgical treatment is instituted immediately, perforation is still the most frequent cause of death in peptic ulcer disease The immediate mortality in perfora- ...

After recovery from the perforation and operation about half of the ... remain symptom free. For a large part of the other half of these patients symptoms and further complications may be anticipated Some patients have had subsequent perforations of peptic ulcers

Subacute Perforation. Spontaneous closure of a perforation is more often present than it is diagnosed The patient exhibits signs of perforation, but soon the symptoms abate, the rigidity disappears, the pulse, temperature and respiration *remain normal, and the rigidity of the abdominal musculature quickly* disappears If the rigidity does not disappear immediately, surgical operation is performed Even if the rigidity disappears, the process may not be over, for the localized peritonitis in the region of the perforation may originate a subphrenic, subhepatic or hepatic abscess as well as localized abscesses in the lesser peritoneal cavity. The occurrence of adhesions may cause partial obstruction of the stomach or duodenum.

The diagnosis is suspected clinically but made by roentgenologic examination

C... ... the serosa, whic... may extend into that organ or tissue Such attachments to the colon, ... der or liver, or *to the pancreas* are common If a peptic ulcer perforates at the site of the attachment to a hollow viscus, a fistula is formed. Walled-off or chronic perforations are associated with one fourth of the intractable ulcers which do not respond satisfactorily to medical treatment The occurrence of adhesions may cause partial obstruction to the outlet of the stomach or to the duodenum

The diagnosis may not be made before operation

stenosis due to peptic ulcer or carcinoma of the pylorus, in children, hypertrophic pyloric stenosis and pyloric atresia of congenital origin The uncommon causes of pyloric obstruction are: prolapse of gastric mucosa or tumor through the pylorus,

passages

Obstructing lesions distal to the papilla of Vater may produce symptoms similar to those of pyloric stenosis due to ulcer The presence of bile in large amounts in the gastric contents of a patient who has a definite gastric retention arouses suspicion that the obstruction is below the papilla of Vater

Symptoms Symptoms at the onset of organic stenosis of the pylorus in a patient who has the history of attacks of ulcer are manifested by a change in the periodicity and character of the pain The characteristic, gnawing type of discomfort of ulcer is supplanted by a feeling of epigastric fullness or heaviness which is worse soon after eating than at other times Anorexia and nausea occur together with regurgitation of the gastric contents The symptoms of pyloric obstruction commence and continue alike in both benign and malignant forms of the disease In either, almost complete obstruction with extreme dilatation of the stomach may be present. In some instances the symptoms of toxemia, malaise, lassitude, asthenia and headache will be more prominent than the symptoms of the obstruction. Retention vomiting, bad taste, anorexia, coated tongue, weakness, thirst, progressive loss of weight, oliguria, and constipation attend all forms of pyloric obstruction Hypochloremia, alkalosis and hyperazotemia ensue

The patient who has an untreated toxemia of pyloric obstruction, often, despite adequate parenteral fluids, may have twitching of the muscles of the mouth, face and extremities, muscle cramps and tetany The patient may sink slowly into a semicomatose condition and die in a state clinically resembling uremia In general, moderate grades of hypochloremia, alkalosis and hyperazotemia do not provoke subjective symptoms other than those attributed to dehydration and yield well to the parenteral administration of electrolytes and dextrose

Examination Evidence of dehydration, dryness of the tongue and skin, may be severe and may suggest uremia There may be evidence of loss of weight In half of these patients visible peristalsis is observed Tapping over the left side of the epigastrium often initiates peristaltic waves if the stomach is not greatly dilated Often a succussion splash may be elicited before breakfast If great toxemia and alkalosis are present, Chvostek's sign and Trousseau's sign may be elicited

Chemical examinations of the blood in those who have pyloric obstruction often reveal the presence of hypochloremia, alkalosis, hyperazotemia and hypopotassemia

During dehydration and alkalosis of pyloric obstruction, urinary excretion is diminished and the urine becomes strongly alkaline from the excretion of bases The excretion of bases depends to some extent on the osmotic pressure of the blood which may be further decreased by the excretion of alkali

The presence of severe dehydration and alkalosis may make it impossible for the kidneys to excrete the urea which is normally produced, so that urea gradually increases until its concentration in the blood is excessive. Hyperazotemia is usually greatest when dehydration is rapid and severe When hyperazotemia is associated with alkalosis, ketone bodies may occur in the urine

In untreated patients the concentration of chloride in the blood continues to decrease, the carbon dioxide combining power of the plasma rises steadily, and the hyperazotemia becomes progressively more severe As the carbon dioxide combining power of the plasma approaches 100 volumes per cent, tetany ensues.

Diagnosis The diagnosis of gastric retention and pyloric obstruction is made by aspiration of the fasting gastric contents and confirmed by roentgenologic exami-

before the operation. Gross hemorrhage in gastrojejunal ulcer is a common event. Melena is more common than hematemesis. Constant slow oozing of blood is the usual method of bleeding. This accounts for the presence of anemia in the patients who have anastomotic ulcer.

EXAMINATION In some patients who have postoperative peptic ulcer there may be no abdominal tenderness In those who have tenderness, it may be elicited immediately above, to the left, but most frequently below the umbilicus. The region of tenderness corresponds to the site of the pain Definite muscle guarding may be present. In some an indefinite tender mass is palpated in the lower part of the epigastrium or in the left central portion of the abdomen

The presence of true achlorhydria practically excludes the diagnosis of gastrojejunal ulcer. The fractional analysis of gastric contents also supplies valuable information concerning the emptying function of the stomach Abnormalities in emptying of the stomach are frequently found, either abnormal delay or rapid emptying

Anemia is a frequent finding

DIAGNOSIS The diagnosis of gastrojejunal ulcer depends on the history and mainly on the roentgenologic examination It may be difficult for the roentgenologist to demonstrate an abnormality in every patient who has an ulcer

In the absence of positive findings a provisional diagnosis of gastrojejunal ulcer should be made in any patient who has ulcer-like distress if a symptom-free period followed an anastomotic operation for a duodenal ulcer If the recurrence of epigastric distress has a rhythm suggestive of ulcer, and if the pain and tenderness are situated lower than those of the original ulcer, a provisional diagnosis of gastrojejunal ulcer is obligatory until it is definitely excluded. Gastroscopic examination of a patient who has undergone subtotal gastrectomy may be difficult and dangerous if attempted by untrained hands.

The prognosis of gastrojejunal ulcer is not good from the standpoint of medical treatment. Radical surgical operation including radical resection of the stomach offers the best prognosis.

Gastrojejunocolic Fistula. In perforation of gastrojejunal ulcer into the colon (gastrojejunocolic fistula) the communication may be a gastrocolic, a jejunocolic, or a gastrojejunocolic fistula These fistulas usually occur in men

The interval between surgical operation and the development of a fistula corresponds to the interval of gastrojejunal ulcer formation The fistula develops soon after the appearance of the symptoms of anastomotic ulcer

In some there are no symptoms of an anastomotic ulcer The onset of the symptoms of a fistulous communication with the colon is characterized by intestinal irritability, a tendency toward frequency and looseness of the stools, and belching of gas having a disagreeable or fecal odor If there is vomiting, the vomitus has a fecal content. Diarrhea is often severe and intractable. If the fistula is small, intestinal symptoms may be slight and intermittent The fecal matter of a patient who has a gastrojejunocolic fistula contains undigested food and increased quantities of fats and soaps Deficiency states, anemia and emaciation may come on with great rapidity as a result of the passage of the food from the stomach directly into the transverse colon. A gastrojejunocolic fistula is suspected in every patient who has undergone a gastroenterostomy and has a spruelike syndrome.

The diagnosis is established by the prompt appearance in the stomach of barium that has been injected into the colon Barium taken by mouth may enter the colon directly. In either case a roentgenogram reveals the barium where it should not be

Obstructions at the Pylorus. An obstruction at the pylorus causes limitations of mobility of the stomach and interferes with the passage of the gastric contents along to the duodenum.

The common causes of pyloric obstruction with gastric retention are. in adults,

duodenal fistula.

Rupture of the Duodenum. In rare instances a blow or crushing injury may rupture the duodenum without external evidence of injury to the abdominal wall Ruptures of the duodenum are commonly due to peptic ulceration A rupture of the duodenum is followed by shock and symptoms and signs characteristic of perforation of a peptic ulcer. The rupture of a viscus is suspected, but its location cannot be determined prior to exploratory laparotomy Plain roentgenograms of the abdomen may reveal pneumoperitoneum The prognosis in all cases of rupture of the duodenum is exceedingly poor

Periduodenitis. The symptoms of periduodenitis are those of the prevailing disease The diagnosis is made at the time of surgical operation

Chronic Duodenal Dilatation and Stasis. Chronic duodenal stasis is an uncertain clinical entity

A few of the symptoms are nausea, belching, and vomiting of bile. Gaseous indigestion, which embraces the sensations of fullness, bloating, discomfort, load or weight in the abdomen coming on after meals and associated with belching, borborygmus and increased flatulence, is present in many cases

Pain, or its equivalent, always is the major complaint Judging from the way it sometimes is described by the patient, the pain, which is situated deep in the epigastrium, closely simulates that of biliary colic Characteristically, the vomiting which is invoked by the patient gives relief

Nervous symptoms and "nervous breakdowns," anxiety, tensional states and various grades of emotional instability are often present An underlying neurosis is responsible for the loss of weight and all of the other symptoms in many of the cases in which chronic duodenal stasis is diagnosed

On examination these patients are of the somatic type having lean and slender body, arms and legs They may be immaculate in personal hygiene and dress. The abdomen is often flabby but rarely pendulous The right kidney can be palpated Tenderness is present everywhere over the body Evidence of avitaminosis and other nutritional deficiencies may be present

A clinical diagnosis of duodenal stasis, consequent to an increased mobility of the duodenum as the result of a long mesentery which permits sagging of the duodenum sufficiently to occlude its lumen, can be made only by those who believe that such a combination of aberrations of anatomy can produce symptoms. Roentgenologically and clinically, there are no definite diagnostic criteria

Carcinoma of the Duodenum. Carcinoma of the duodenum is rare, and if it occurs, the second portion of the duodenum is the most frequent site The manifestations of duodenal carcinoma depend on the situation of the tumor The presumptive diagnosis is made by the roentgenologist and confirmed by histologic study of biopsied tissue

Carcinoma of the Ampulla of Vater. Carcinoma of the ampulla of Vater may be situated in the supra-ampullary, periampullary or infra-ampullary regions

A growth in the supra-ampullary region often produces the symptoms of a duodenal ulcer Obstruction near the pylorus eventually ensues Invasion of the duodenal wall in the supra-ampullary portion may encroach on the common bile duct and main pancreatic duct, causing a progressively intense jaundice The diagnosis may be established by roentgenologic examination but more commonly is confirmed at the time of surgical exploration

A carcinoma situated close to the ampulla of Vater is often associated with intestinal bleeding and with jaundice. There may be postprandial epigastric discomfort A jaundice of fluctuating intensity associated with intestinal bleeding is

nation. The volume of the fasting gastric contents exceeds 100 ml. and may reach several liters. The stomach often contains undigested items of food taken one or more days prior to aspiration The cause of the pyloric obstruction may be determined by roentgenologic examination. The barium meal should be removed by aspiration immediately after the examination

DISEASES OF THE DUODENUM (EXCLUSIVE OF PEPTIC ULCER)

The common disease of the duodenum, peptic ulcer, has been considered. Likewise some of the important congenital anomalies have been discussed. Here will be described some diseases of the duodenum, perhaps generally regarded as rare, but real to the patients who have them.

The duodenum is composed of four portions The first portion (superior) begins at the pylorus and ends at the neck of the gallbladder. It is about 2 inches (5.1 cm) long, and runs backward along the body of the first lumbar vertebra. The second portion (descending) is about 4 inches (10 2 cm.) long, and runs down the right side of the bodies of the lumbar vertebrae to the lower border of the third vertebra. The third portion (variously called ascending, transverse or inferior) runs diagonally upward across the body of the third lumbar vertebra to its left side, and then the fourth portion ascends to the left side of the second lumbar vertebra, where it takes a sharp turn and is continued as the jejunum.

Duodenitis and Gastroduodenitis. Acute or chronic duodenitis often is but part of a widespread mucosal inflammation in either the stomach or the small intestine, or it has developed as a result of obstruction or of peptic ulcer in the duodenum It does exist alone as an entity

The term *gastroduodenitis* is employed to describe the inflammatory condition of the duodenal mucosa which may occur in association with chronic gastritis.

Duodenitis may result from direct irritation of the duodenum, as from *Ancylostoma duodenale* (hookworm), from a diverticulum, or from disease of contiguous organs

Superficial erosions appear in the duodenum in association with severe cutaneous burns, uremia, tumors of the cerebrum or midbrain, portal hypertension, or congestive heart failure or from drugs given to abate heart failure. The only definite evidence of the presence of these erosions is melena, which at times is severe In a few cases in which there are subjective symptoms, they are no different from symptoms of simple duodenal ulcer

Judd and Nagel recorded instances of duodenitis which seemed to be a separate entity. In these cases there were congestion and stippling of the serosa of the duodenum without appreciable induration of its wall. The mucosa was the seat of a circumscribed or diffuse inflammation The duodenum was not ulcerated In some cases small discrete abrasions were present. The patients, most of them aging men, all presented themselves for examination and operation for profuse and repeated gastrointestinal hemorrhages Prior to operation the results of all examinations, except for evidence of varying degrees of anemia, were negative

The diagnosis of duodenitis is established by surgical exploration, in which the duodenum is opened to determine the origin of the melena. The prognosis is good.

Tuberculosis of the Duodenum. In the late stage of tuberculosis, achlorhydria may result from gastroduodenitis Occasionally, in the ulcerative type of intestinal tuberculosis, the duodenum may be involved and, in rare instances, isolated tuberculous lesions occur in the duodenum. Tuberculosis of the duodenum may occur in association with obstructing malignant lesions. Tuberculosis of the duodenum is clinically nondiagnosable

Duodenal Fistulas. There are no symptoms referable to duodenal fistula The symptoms present are those referable to the disease conditions causing the fistula, such as perforations of the gallbladder, peptic ulcer, carcinoma of the stomach or the colon, and perforation from direct injury.

Allergy is a cause of intestinal disorders but its exact manifestations are difficult to define (see Allergic State, Chapter 18).

A failure of absorption of the intestinal chyme is present in those ill-defined conditions known as idiopathic steatorrhea, sprue and coeliac disease. It seems that in some instances a deprivation of vitamins may be due to failure of intestinal absorption. The known examples of failure of intestinal absorption are manifested by diarrhea, usually steatorrhea and a macrocytic anemia. A failure of absorption may be incident to removal of long segments of the intestines or exclusion of comparably long segments by anastomotic operations.

Pain when due to disease of the small intestines is often of intermittent character and situated about the umbilicus In disease of the colon pain is more nearly situated over the site of the disease.

The most significant manifestation of disease of the small intestine is loss of body weight In malignancy of the small intestines a rapid loss of body weight is almost always present

Diseases of the Intestines Due to Prenatal Influences. Whether or not a particular departure from the normal shape, position, size, length and state of fixation of segments or the whole of the intestine is a predisposing cause of acquired organic disease is not always possible to evaluate Many of these departures are known to be the result of congenital malformations and are without significance

That part of the intestine derived from the primitive midgut is more liable to developmental defects than any other part of the alimentary tract Congenital abnormalities are commonest (1) at or just distal to the junction of the primitive foregut and midgut, which is represented in postnatal life by the descending duodenum, (2) in the terminal ileum in the region of attachment of the embryonal omphalomesenteric duct and (3) in the cecum and ascending colon to the midtransverse colon where the primitive midgut ended

The small intestine lengthens rapidly In the embryo of 7 weeks the intestinal loop protrudes into the umbilical cord, forming a normal umbilical hernia

The large intestine grows much more slowly than the small intestine during this period In embryos of 10 weeks the abdominal cavity has grown sufficiently large so that the intestine can return The return is accomplished suddenly The small intestine is the first to re-enter the abdomen It does this in a progressive manner, the proximal portions leading, the returning coils pass behind the outstretched mesenteric artery and fill the available space on the left side of the abdomen This return of the intestine to the abdominal cavity is known as *intestinal rotation*

The large intestine is the last to leave the umbilical cord and re-enter the abdominal cavity. Its tendency to straighten, because of its thickness, then carries the cecum across to the right side of the abdomen just under the underedge of the liver, where it may remain Usually at birth, however, or by the end of the first year of life the cecum has descended to the crest of the ilium, and here it becomes fixed From this point the colon passes obliquely upward to the left of the stomach, where it recurves sharply into the future descending colon. The latter limb, remaining on the left side, forms the sigmoid segment to the midplane, where it joins the rectum As the liver loses in relative size in the enlarging abdominal cavity, a hepatic flexure appears in the originally oblique proximal limb of the colon

The ascending colon, beginning to elongate as such in the middle of fetal life, is not completed until early childhood The original cecal bulge grows and makes a definite, blind sac that extends the large intestine beyond its junction with the ileum The distal end of this sac lengthens so that the vermiform process, the appendix of the higher apes and man, becomes distinct from the cecum The cecum forms a U-shaped bend with the colon proper at 10 weeks, and this flexure with its inwardly folded walls is responsible for the ileocecal valve (valvula coli) Just distal to this valve two diverticula form and during their formation the appendix is rotated to its normal posterior position The transverse colon courses ventral to the duodenum The descending colon, like the ascend-

often due to carcinoma of the region of the papilla of Vater. On examination the gallbladder and the liver may be palpable The roentgenologic findings may be inconclusive. Anemia is usually present If gross blood is recovered from the duodenum on duodenal intubation, this may supply the first implication of the diagnosis

Carcinoma arising in the fourth portion of the duodenum, or infra-ampullary region, near the duodenojejunal junction may be manifested by the symptoms and signs of duodenal stasis On examination there is a palpable mass. The patient is pale Anemia is present. The diagnosis is established by roentgenologic examination

THE JEJUNUM AND ILEUM

(*The Small Intestine*)

The small intestine is composed of the jejunum (the empty portion of the small intestine) and the duodenum and the ileum The jejunum is about 8½ feet (2.59 meters) long and the ileum about 12½ feet (3 81 meters) They are bound to the spinal column by the mesentery, which extends from the left side of the body of the second lumbar vertebra to the right sacro-iliac joint

The jejunum and the ileum participate with the stomach, the duodenum and the colon in some acute infections such as acute gastroenterocolitis They bear the brunt of many of the diseases due to the animal parasites and often share with the colon some of the burdens of diseases of unknown causes such as ileitis and ileocolitis In addition to these diseases they have major diseases of their own Here the major diseases of the jejunum and ileum will be considered which are not described in association with diseases of the stomach, duodenum and colon

Manifestations of Disease. The manifestations of disease of the mesenteric small intestine may be enumerated as: (1) motor dysfunctions and obstruction, (2) inflammations and fevers, (3) hemorrhage, (4) allergy, (5) failures of absorption, (6) pain and (7) weight loss

Motor dysfunction may be manifested by noisy peristaltic movements—borborygmus Borborygmus often indicates a heightened peristaltic activity. If a mechanical intestinal obstruction is present there is constipation In the absence of mechanical obstruction often there is diarrhea

Diarrhea is by far the most common manifestation of disease of the intestines distal to the duodenum Diarrhea may be either acute or chronic. Acute diarrheas attend many acute infectious processes in the intestines and food poisoning The chronic diarrheas are due either to intrinsic disease of the intestines or factors extrinsic to the intestines These extrinsic factors may originate in parts of the digestive tract away from the intestines For example, may be enumerated. gastrogenous, such as that incident to achylia, achlorhydria, gastritis, gastroenterogenous fistulas, pancreatic disease, biliary tract disease, and perhaps the most common of all, the nervous diarrheas of functional origin

The intrinsic diarrheas are due to disease of the intestines. The causes for intrinsic diarrheas may be categorically arranged as follows. (1) infections which include all the agents of infection such as bacteria, viruses, and higher animal and plant parasites, (2) diseases of unknown causes such as chronic ileitis and chronic ulcerative colitis and (3) neoplasms both benign and malignant.

During the course of chronic infections and fevers there may be intestinal dysfunction The dysfunction may be due to direct involvement of the intestine by the infection or it may be due to some unknown cause related to the infection. An example of the latter may be cited: the acute episodes of diarrhea which often attend subacute or chronic bacterial endocarditis

Hemorrhage, blood appearing in the bowel motion as dark greasy black material, may be the only manifestation of ulcerative lesions or malignancy of the small intestines or proximal colon.

The diagnosis of congenital atresia is suggested by the onset of persistent vomiting immediately after birth. Roentgenograms reveal a complete obstruction of the second portion of the duodenum. Congenital atresia of the duodenum must be differentiated from congenital pyloric stenosis

Meckel's Diverticulum. This much publicized congenital outpouching of the ileum is a remnant of the omphalomesenteric duct, connecting the primitive intestine with the umbilical vesicle (Fig 13-3). This duct should close between the third and fifth weeks of fetal life. It may not close at all, and if not, a fistula remains in the abdominal wall below the umbilicus (see the Umbilicus, p. 882) through which feces may pass. An abdominal fistula may persist with the ileum in direct communication with the opening at the umbilicus The ventral fissure may close, but a blind process of the ileum persists which is united to the umbilicus by the obliterated duct represented as a solid fibrous cord

The usual deformity, however, is a persistence of the omphalomesenteric duct as a free diverticulum from the ileum This free diverticulum (Meckel's diverticulum) varies greatly in length It is situated in the ileum somewhere above the ileocecal junction and projects from the free border of the ileum The lumen may be as large as that of the ileum

Heterotopic gastric, pancreatic, or duodenal mucosa may be present in Meckel's diverticulum Aberrant gastric mucosa capable of secreting a potent gastric digestive juice is said to account for the occurrence of peptic ulcer in these pouches The ulcer is often found in the intestinal mucosa bordering on the heterotopic gastric mucosa

Symptoms are rarely caused by Meckel's diverticulum, but when present they often result from an inflammation and simulate the symptoms of appendicitis Perforation may occur and peritonitis ensue Occasionally perforation, volvulus and gangrene, or intestinal obstruction, may occur The diverticulum may become adherent within a hernial sac Hemorrhage or perforation of the peptic ulcer may occur The hemorrhage may be acute and severe or the bleeding may be repeated until severe macrocytic anemia is present Tumors such as fibrosarcomas, leiomyosarcomas, carcinomas, carcinoids and adenomas have been reported in Meckel's diverticulum

Diagnosis of a diseased Meckel's diverticulum is established by exclusion A hypochromic macrocytic anemia present in a young adult who has abdominal symptoms is suggestive of a bleeding Meckel's diverticulum The anemia may occur without other symptoms The confirmation is had at the time of surgical exploration because of indeterminate intestinal bleeding or in cases in which appendicitis is suspected Most Meckel's diverticula are found at postmortem examination and have been devoid of disease

Anomalies of Fixation. There are many departures from the average normal arrangement of intestinal attachments, especially of colonic attachments Normal functioning of the small intestine and the colon proceeds independently of position and degree of mobility

Volvulus of the Small Intestine Congenital or acquired defects of the intestine or its mesentery may contribute to the development of volvulus in the small intestine

There are several embryonic defects which are factors in producing this anomaly. Short attachment of the root of the mesentery may cause volvulus, particularly if the short attachment is in the long axis of the body The mesentery may be too long, without the usual points of fixation

The acquired defects are usually of inflammatory origin causing irregular segmental shortening of the mesentery, and they may lead to a contraction which is conducive to volvulus

In 37 cases in which operation was performed, McKechnie and Priestley listed the incidence of volvulus attributable to the various causes as follows: (1) acquired causes (26 cases), (2) congenital causes (8 cases) and (3) idiopathic (3 cases).

The distal portion of the ileum is the segment of the intestine most frequently

ing limb, is applied against the body wall and each loses its free mesentery to become fixed.

Proliferation of the epithelial lining of the duodenum leads to its occlusion in the sixth and seventh weeks, but vacuolation soon restores the lumen. The remainder of the small and all of the large intestine show a similar phenomenon, but in lesser degree

Anomalies of Rotation of the Intestines. Wide variations in the degree of nonrotation of the intestines are observed. Unless there is some deformity in addition to nonrotation which permits of or produces intestinal obstruction, nonrotation is compatible with digestive health

At the time of surgical operation inside of the abdomen or during roentgenologic study of the intestine the second part of the duodenum may be observed to turn toward the right rather than to the left, and the jejunal loops are seen in the upper right portion of the abdomen instead of in the upper left portion. It is commoner, however, to observe a failure of rotation which involves only the colon. It is presumed that in these cases the colon returns to the abdominal cavity first from the umbilical hernia

Anomalies of Position of the Intestines. No symptoms are assigned to a *duodenum* that is out of place and varies in its degree of mobility The presence of the duodenal mesentery, which permits of free mobility, often described as an inverted duodenum, likewise is free of symptoms

A double point of fixation of the duodenum, forming a redundant loop, in itself is symptomless If symptoms are present, they are due usually to a periduodenitis from a perforated ulcer

A *cecum* fixed under the liver or anywhere along the right side of the abdomen is symptomless A cecum and a *colon* all on the left side of the abdomen are likewise symptomless.

Excessively *long colons* (dolichocolons) or excessively long *sigmoidal loops* (dolichosigmoids) are symptomless

Intestinal Bands and Membranes. Congenital membranes or bands extending from the region of the gallbladder and undersurface of the liver to the proximal duodenum are seen in three forms. (1) a veil or membrane occupying the same general position as the cysticoduodenal ligament, (2) firm bands extending from the duodenal cap to the region of the anterior border of the left lobe of the liver and (3) bands extending from the superior surface of the mesocolon to the upper part of the duodenum or the pyloric region.

A congenital peritoneal band or membrane extending from the antimesenteric border of the ileum to the right iliac fossa causes a kink (*Lane's kink*) in the distal terminal ileum which may be observed by the roentgenologists Lane's kink causes no symptoms

In infants these bands, with the exception of Lane's kink, may be associated with symptoms of pyloric obstruction similar to those produced by congenital hypertrophic stenosis. There are dilatation of the stomach, visible gastric peristalsis, and emaciation A tumor is not present

The diagnosis of intestinal bands and membranes or their differentiation from periduodenal bands and congenital duodenal atresia is not possible except by surgical exploration

Congenital Atresia of the Small Intestine. Atresia may be found in any part of the small intestine. The three common sites are the second portion of the duodenum, the duodenojejunal junction, and the lower part of the ileum

Atresia of the Duodenum The common site of atresia of the duodenum is proximal to the ampulla of Vater, corresponding to the juncture of the primitive foregut and midgut, near the site of occurrence of the embryonal rotation of the small intestine. Atresia in this location may be due to the persistence of physiologic epithelial occlusion, which has been mentioned as being present normally between the first and second months of embryonal life

Diverticula of the Intestines. An intestinal diverticulum is a hernial protrusion of the mucosa of the intestine through the muscular coat.

Diverticula of the *duodenum* are of common occurrence. Duodenal diverticula are usually single, vary in size, and project from the pancreatic border of the duodenal curve in the second, third and fourth portions of the duodenum Multiple diverticula of the duodenum occur more commonly in patients who have diverticula in other segments of the alimentary tract than in those who do not

There is much evidence to support the existence of a congenital weakness in the duodenal wall which probably results from the normal process of vacuolation in the normal restoration of the lumen The larger pouches usually lack a muscular coat, although very often the smaller ones do contain some muscle fibers.

Symptoms are lacking Diagnosis is made by roentgenologic examination There is little evidence to support the diagnosis of duodenal hemorrhage from a diverticulum if peptic ulceration is not present The roentgenogram alone renders a clinical diagnosis possible but does not imply that the abdominal symptoms are due to diverticula.

Usually treatment is not necessary for these diverticula

Diverticulosis of Small Intestine. Diverticula in the small intestine are infrequent. They may occur, however, singly or multiply in the *jejunum* and in the terminal portion of the *ileum* and they vary in size

Single diverticula of the small intestine, often called pulsion diverticula, develop at points of weakness in the intestinal wall The origin of multiple diverticula is probably related to congenital faults similar to those of the duodenum These diverticula are commoner in men than in women

The symptoms of diverticula of the small intestines, if any are present, are abdominal pain, occurring at any time, fever, and low-grade intestinal obstruction indicated by abdominal distention, vomiting and constipation Bleeding may occur and at times the hemorrhage is severe Localized peritonitis occurs in some cases, and perforation of the bowel has been recorded Acute diverticulitis necessitating an emergency operation has been observed The pouch may become strangulated and gangrenous

The symptoms of intestinal diverticulosis when present are not distinctive They may simulate many other lesions The diagnosis is made by roentgenologic examination or at the time of surgical exploration

Diverticulosis of the Colon. A colonic diverticulum is the protrusion or herniation of the mucosal membrane through the muscular coat of the colon, forming a permanent sac. When outpouchings of this kind are present without being inflamed, the condition is designated diverticulosis of the colon Diverticulosis of the colon often exists indefinitely without recognizable symptoms

The cause of colonic diverticulosis is unknown At this time it is impossible to rule out a predisposing weakness in the involved part. Perhaps there is an increased intracolonic pressure in addition to the innate weakness to account for the formation of colonic diverticula

Colonic diverticula are semiglobular and communicate with the colonic lumen by necks of varying sizes The diverticula vary in size from a barely visible pouch to a sac 2 to 4 cm in diameter Diverticula rarely occur in the rectum, but the proctologist frequently views them in the distal portion of sigmoid They are situated close to the mesenteric attachment and often are confined to the appendices epiploicae and the sigmoid segment of the colon Frequently they are widely disseminated through the colon

Diverticula are in close relation to the blood vessels as the vessels pass through the muscular coat, and they may appear on the lateral and the antimesenteric aspects of the bowel The number of colonic diverticula increases as time passes.

The incidence of diverticulosis of the colon is unknown. The process of diverticularization seems to begin around the age of 40 years but persons less than the age

involved. The extent of the volvulus is limited by the degree of rotation permitted The pathologic changes are limited by the extent of injury to the mesentery.

When the circulation is grossly impaired, there are local hemorrhages, necrosis and gangrene of the bowel as the final results Peritonitis is a common complication of severe strangulation In those in whom strangulation is an early development and gangrene and perforation of the bowel follow quickly, shock, high fever, chills and general peritonitis ensue In cases in which volvulus is intermittent, the periods between complete occlusion may be marked by diarrhea In others, less than one half, obstipation is present The disease is more common in adults than in children

On examination, there are abdominal distention, tenderness and rigidity. Generally the findings are characteristic only of sudden acute intestinal obstruction These patients are often critically ill

The clinical symptoms and the findings on examination are usually not sufficient to enable one to make a preoperative diagnosis of volvulus. The diagnosis is surgical.

Volvulus of the Colon The *cecum* is commonly involved by volvulus due to congenital faults Imperfections in rotation may permit of volvulus in the newborn or in later life However, volvulus of the cecum seems to be more directly related to errors in descent and fixation of the cecum and ascending colon than to failures in rotation This does not imply that all mobile ceca will become involved in volvulus, but rather that if volvulus does occur a mobile cecum is a prerequisite.

Volvulus in the cecum commences at the point where the lack of fixation of the bowel begins The degree of rotation varies; several twists may occur Full rotation may occur without vascular occlusion The involved cecum may be found in any part of the abdomen The cecum is usually extremely distended after volvulus occurs

The symptoms of volvulus of the cecum are not characteristic. There may be pain in the lower part of the right side of the abdomen, borborygmi and constipation Chronic and recurring cecal volvulus may occur as attacks of pain in the right lower quadrant of short duration without tenderness

Examination of the abdomen in volvulus of the cecum reveals tenderness, some distention in the right lower quadrant and, in an occasional instance, a palpable mass there.

The diagnosis of volvulus of the cecum is not made prior to operation

Volvulus of the *sigmoid* often occurs when there is a long sigmoid with excessive mobility.

An abnormally long sigmoid flexure (dolichosigmoid) is frequently reported by the roentgenologist in those who have had no significant bowel trouble

Sigmoidal volvulus is rare in childhood. It occurs chiefly among elderly men In the majority of cases the patients are between 40 and 70 years of age, the average about 60 years

The onset is sudden Pain is localized to the left lower abdominal quadrant. The rectum is emptied soon after the volvulus occurs and thereafter no feces or flatus is passed Abdominal distention develops rapidly.

When the onset is acute, collapse and shock are often present In some patients, however, the symptoms may fluctuate for a number of days and then disappear. At any time during this period of fluctuation there may be a sudden transition to an illness of great severity with acute pain, abdominal distention and shock Once the acute symptoms due to volvulus have been established, there is an increasing distention and, finally, the features of peritonitis appear

On bimanual examination a tender soft pelvic mass may be palpated

The diagnosis is usually made at the time of surgical exploration

The mortality rate of surgical treatment of volvulus is high. The operative mortality in volvulus of the sigmoid is greater than in any other type of volvulus

Volvulus often recurs after operation, and often requires reoperation.

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The diagnosis is usually made at the time of surgical exploration

The mortality rate of surgical treatment of volvulus is high The operative mortality in volvulus of the sigmoid is greater than in any other type of volvulus

Volvulus often recurs after operation, and often requires reoperation.

vention is reserved for cases in which there are complications or sequelae or both.

According to Brown it is impossible to predict which individuals will have diverticulitis of a mild degree or which will have severe symptoms and will require surgical intervention

COMPLICATIONS OF DIVERTICULITIS OF THE COLON. The complications of diverticulitis comprise. (1) acute perforation into the free peritoneal cavity, (2) peridiverticulitis, (3) localized peritonitis, (4) abscess formation and (5) rupture of abscess with an ensuing fistula

Free perforation into the peritoneal cavity, causing acute peritonitis, is rare The signs and symptoms of a free perforation are shock, severe generalized abdominal pain, and a rigid, silent abdomen. The usual course is slow perforation with abscess formation, in which case the signs and symptoms are less severe than when free perforation is present, and there is local peritonitis Often such abscesses are absorbed In other instances the abscess enlarges sufficiently to obstruct the bowel The abscess may not obstruct the bowel but may rupture into adjacent organs and form entero-intestinal, enterovesical, or enterocutaneous fistulas. A less serious complication of diverticulitis is a scarring constriction of the lumen. This complication often follows many and repeated attacks of diverticulitis.

In some there seems to be a considerable spasm of the bowel revealed by a constriction of the colonic lumen on roentgenologic examination. These patients may have a longer convalescence from an attack than is expected It seems therefore reasonable to assume that there is considerable *peridiverticulitis* present.

Local peritonitis commonly appears in association with acute diverticulitis If the inflamed diverticulum is embedded in an epiploic appendage the latter structure may participate in the reaction, possibly contributing to the peridiverticular inflammatory reaction The presence of pus usually causes a marked change in the manifestations In addition to the fever and leukocyte response, there may be evidence of an abscess near the site of the lesion The local signs of rigidity and pain may become more marked Occasionally the abscess may rupture into the general peritoneal cavity, in which case a generalized peritonitis develops More commonly, however, the abscess becomes absorbed If resolution does not take place the abscess ruptures into a neighboring organ, for instance the intestine (entero-intestinal fistula), the bladder (enterovesical fistula), the surface of the body (enterocutaneous fistula) or the vagina (enterovaginal fistula).

The patient is often first seen on account of one or more of these complications Usually there is a preceding history of attacks of acute diverticulitis, but there may not be

On examination there are localized tenderness in the left lower abdominal quadrant and leukocytosis Soon there is a tender mass near the site of the peritoneal soiling. The local signs of rigidity and pain are definite.

As stated, *fistulas* are complications resulting from rupture of abscesses. The common fistula is a communication between the colon and the abscess cavity. The track of such a fistula is discovered on roentgenologic examination after the acute symptoms have subsided Fistulous communications are sometimes established with the urinary bladder and with other segments of the intestines (Fig. 7-2, p 403).

The *vesicocolonic fistulas* give definite symptoms. The sigmoid colon is anatomically posterior to the urinary bladder. The common site for vesicocolonic fistula from a perforated diverticulum of the colon is the posterior wall of the bladder.

The chief symptom of vesicocolonic fistula is the passage of flatus and feces through the urethra There are urinary frequency and urgency and often a burning pain in the bladder. These symptoms may or may not have been preceded by those of an existing diverticulitis. In some the diverticulitis has been troublesome prior to the vesical complication In a few men the first noticeable symptom of a vesicocolonic fistula or of the diverticulitis may be the passage of flatus through the penis.

of 30 years may have the disease. Diverticulosis seems to be about equally distributed between men and women.

Those who have diverticulosis do not belong to any one somatic type. The bowel habit prior to diverticulosis is not characteristic

There are no symptoms which can be attributed to colonic diverticulosis.

Diverticulosis is discovered in the course of a routine roentgenologic examination of the colon or at the time of abdominal operation for other intra-abdominal causes.

Diverticulitis of the Colon. Diverticulitis is inflammation of a diverticulum The symptoms of diverticulitis depend on the degree of inflammation and the nature of the complications Brown's experience indicates that in one third of those who have diverticulitis the symptoms can be attributed to inflammation, either acute or chronic, and that in two thirds they result from inflammation plus obstruction

Three fourths of patients who have diverticulitis are between the ages of 50 and 60 years when the condition is discovered. The disease affects equally both men and women There are no race exemptions

Acute Diverticulitis of the Colon Acute inflammation or acute diverticulitis may involve any portion of the colon but, like diverticulosis, it occurs most commonly in the sigmoid flexure Formerly it was called left-sided appendicitis because of certain resemblances of the signs and symptoms to those of acute appendicitis There is pain in the left lower part of the abdomen, rarely nausea or vomiting; usually the bowels are constipated

The symptoms may persist for one or two days, followed by resolution, or the process may continue and one or more of a number of complications may ensue.

The patient has fever, tenderness and muscle guarding, but rarely rigidity of the muscles There is often an increased leukocyte count

Usually if diverticulitis is present, the roentgenologist recognizes the condition by certain criteria and will report it The history and examination may be the deciding points in favor of diagnosis of diverticulitis

Recurring Diverticulitis of the Colon Recurrent attacks of acute diverticulitis almost invariably indicate the presence of some complication, the nature of which will vary in individual cases

Chronic Diverticulitis In chronic diverticulitis there is an increased interruption of the normal colonic function as a result of inflammatory reaction in the colon and contiguous structures Usually there has developed a marked inflammatory hyperplasia with partial intermittent colonic obstruction in association with adhesions A mass may be present at the site of the inflammatory reaction, usually in the lower left quadrant The signs and symptoms of low-grade intermittent obstruction may intervene. Later, in rare instances, complete colonic obstruction supervenes with all the phenomena of that condition.

DIAGNOSIS OF DIVERTICULITIS The diagnosis is usually established by roentgenologic examination However, there are instances of subacute abscess formation in which there is no other evidence of diverticular disease

The passage of gross blood in the feces in the absence of hemorrhoids and fissures is rare in diverticular disease When there is gross blood in the feces in this condition, search should be made for a coexisting polyp or a cancer

Diverticulitis and cancer are common in persons of the same age group. The occurrence of these two diseases in the same person is no more than coincidental Often a subacute perforating carcinoma of the sigmoid and diverticulosis may coexist and thus cause preoperative diagnostic difficulties. Subacute perforating diverticulitis and a subacute perforating carcinoma are both to be treated surgically Preoperative diagnosis is preferable but not always possible or essential.

The prognosis depends on the degree of disease and the success of the treatment required when the patient is first examined Basically the treatment of diverticulosis and mild diverticular disease is medical, and the prognosis is good. Surgical inter-

longitudinal ulcers also occur. The encircling tendency may account for partial intestinal obstruction Intestinal obstruction, however, is more often the result of serosal involvement with localized peritonitis and kinking of the intestine than of actual stenosis of its lumen. Peritonitis may develop as a late complication Perforation occurs most often in the ileum and next in frequency in the appendix The formation of fistula often follows operative procedures

SYMPTOMS. Often the only symptoms of a pulmonary tuberculosis are manifested by intestinal dysfunction such as an irritable colon, gastric dysfunction and anorexia

Those who know pulmonary tuberculosis and have observed its complications suspect the existence of intestinal tuberculosis if constant intestinal symptoms arise in the presence of an irregularity in the daily temperature which is not explained by the course of the pulmonary lesion and a continued unsatisfactory progress, characterized by a failure to gain weight, attended by abdominal discomforts and aberrations in regularity of bowel motions

The abdominal pain is vague, generalized, and often somewhat relieved by defecation As the condition worsens, the pain is severe. A localized, severe, constant type of pain is present when there is peritoneal irritation.

A persistent diarrhea arouses the suspicion of tuberculous involvement of the intestine in any patient who has active pulmonary tuberculosis Gross mucus, pus and blood are not commonly found in the feces Massive hemorrhage from the intestine is extremely rare.

EXAMINATION. The examination of the abdomen of a patient who has intestinal tuberculosis may not reveal abnormality With the advent of intestinal obstruction, abdominal distention occurs, and very often isolated loops of small intestine may be palpated in the abdomen or may be seen through the abdominal wall A circumscribed mass is rarely palpated in ulcerative intestinal tuberculosis

DIAGNOSIS Roentgenologic study affords the only means of clinical diagnosis of ulcerative intestinal tuberculosis prior to histologic examination and inoculation of guinea pigs with infected material.

Hypertrophic Tuberculosis This form of intestinal tuberculosis is known also as hyperplastic, nodular, scirrhous intestinal tuberculosis, neoplastic cecal tuberculosis and intestinal tuberculoma The disease frequently occurs in the absence of active pulmonary tuberculosis

Hypertrophic intestinal tuberculosis is characterized by hyperplasia of fibrous tissue and extensive thickening of the wall of the intestine with some degree of narrowing of its lumen The lesion tends to remain sharply localized

There is often an aching type of pain in the right side of the abdomen. The patient hears much gurgling of gas A bowel motion may give temporary relief from these symptoms. Pressure at times tends to relieve the pain and thus the patient discovers a mass There is some loss of weight as a result of a decreasing appetite.

On examination the tumor is hard and moderately fixed in the right side of the abdomen. Results of the rest of the examination, including that of the lungs, may be negative.

[illegible]

followed by rest and food

Intestinal Granulomas. The term granuloma designates a tumor which arises as a result of the continuous action of an irritant, provoking the formation of an excessive amount of inflammatory tissue. Intestinal granulomas are rare. There are specific granulomas, which arise during the course of an infection by a known agent, such as *Treponema pallidum*, the tubercle bacillus, or most commonly, *Endamoeba histolytica* There are nonspecific granulomas arising as the result of an unknown

Following the onset the urinary symptoms of dysuria, frequency, urgency and the passage of liquid feces may be of no great consequence or may cause severe discomfort. In time the urinary infection may become severe.

Entero-intestinal fistulas often result from perforation of the abscess back into the intestine In such case a large quantity of pus is emptied into the intestinal lumen and passed in the bowel motion. If pus is not passed with the stool, there are no other symptoms which indicate this complication These fistulas may heal spontaneously.

In women *enterovaginal fistulas* are commoner than fistulas into the bladder. Enterovaginal fistulas are manifested by the passage of gas, feces and pus from the vagina.

External fistulas rarely form anywhere else except in the vagina.

Infections of the Intestines. *Acute Enteritis.* Acute enteritis is divided into four large categories. (1) acute enteritis due to increased susceptibilities, (2) acute enteritis due to bacteria and viruses, (3) acute enteritis due to food poisoning from chemicals and (4) acute enteritis due to food poisoning from plants and animals. These conditions are described in their appropriate places in this text.

Chronic Enteritis. The diagnosis of chronic enteritis generally is a sort of escape from reality, for tuberculous enteritis, nonspecific regional enteritis, and the dysenteries are the only diagnosable diseases which fulfill any reasonable definition of chronic enteritis Despite these common observations the diagnosis of chronic enteritis often is made When such a diagnosis is assigned, it is realized that the patient has a chronic enteritis which may have originated from an addiction to alcohol which has caused chronic gastritis and finally achlorhydria and vitamin deficiency disease, or perhaps too much condiments, food roughage, or irritating medicines have been ingested. In some instances strong laxatives and cathartics have been administered for intractable constipation.

There is a chronic diarrhea of long duration associated with generalized abdominal pain or discomfort. The description of the stools is that of any stool passed as one in a series of evacuations in a day mushy, voluminous, but free from pus or blood Often excessive mucus is present.

There is no real pain. The complaint is a feeling of distention, bloating or fullness, a crampy sensation, or a feeling of moving gas Nutritional deficiencies are present in the severe instance of chronic enteritis. The results of physical examination and roentgenologic examination are negative

A diagnosis of chronic enteritis is made after ulcerative colitis, amebic colitis, *diverticulitis, polyposis and early malignant lesions, tuberculosis of the small intestine*, pernicious anemia, nontropical sprue and deficiency states, tumors, and obstructions in the small intestine have been ruled out

Tuberculosis of the Intestines. Intestinal tuberculosis occurs in two main forms, ulcerative and hypertrophic.

Ulcerative Tuberculosis This form of intestinal tuberculosis most commonly occurs in the presence of advanced pulmonary tuberculosis, and is most frequent in patients between the ages of 20 and 40 years. The incidence diminishes and the degree of involvement is less in patients more than 40 years old.

The incidence of involvement of the intestines increases as the activity of the pulmonary processes widens and as the sputum becomes filled with tubercle bacilli, which are swallowed Some phthisiologists have looked favorably upon a hematogenous pathway of infection, but the clinical evidence supports belief that the germs are swallowed.

The earliest lesions occur in Peyer's patches and in solitary lymph follicles in the wall of the intestine. The overlying mucous membrane becomes swollen and may slough, leaving an irregular-edged ulcer. Tuberculous ulcers tend to encircle the bowel, though

The cyclophyllidean tapeworms of man belong to the superfamily Taenioidea. Five families are of economic and medical importance: Anoplocephalidae, Davaineidae, Dilepididae, Hymenolepididae and Taeniidae, the last two including important parasites of man.

Dwarf Tapeworm Infection. In man this infection is caused by species *Hymenolepis nana, Hymenolepis diminuta* and *Drepanidotaenia lanceolata,* members of the family Hymenolepididae. Only the first two are of medical importance

Hymenolepis nana is a common tapeworm of man in the southern United States. It infests mice and rats also No intermediate host is required for the life cycle of this worm The infection is transmitted directly from hand to mouth

Hymenolepis diminuta produces pathologic changes similar to those caused by *Hymenolepis nana* However, *Hymenolepis diminuta* requires an intermediate host for development The natural definitive hosts of *Hymenolepis diminuta* are rats and mice. Man and dogs are accidental hosts The principal natural intermediate hosts are the rat fleas (*Ceratophyllus fasciatus* and *Xenopsylla cheopis*), which are infected in the larval stage, and the meal worm beetle (*Tenebrio molitor*).

These worms inhabit the *proximal portion* of the *ileum* without material injury to the mucosa. Light infections produce no symptoms Children who have many of these parasites may have abdominal pain with or without diarrhea, dizziness, strabismus, headache, epileptiform convulsions, and nervous disturbances. The blood may show a decrease in erythrocytes and hemoglobin, and in most instances there is an eosinophilia of from 4 to 16 per cent.

Diagnosis is based on finding the characteristic ova in the feces. The prognosis is favorable with or without treatment.

Infection with Taenia Three species of the family Taeniidae, superfamily Taenioidea, genus *Taenia,* are important parasites of man These are the pork tapeworm, *Taenia solium;* the beef tapeworm, *Taenia saginata,* and the hydatid tapeworm, *Echinococcus granulosus* The adult taenial worms are parasites of carnivorous or omnivorous animals and the larvae are parasites of herbivorous or omnivorous animals.

1. The Pork Tapeworm. Human infection with the pork tapeworm, *Taenia solium,* is especially prevalent where raw or insufficiently cooked pork is consumed. The adult parasite is extremely rare in man in the United States of America, although cysticerci are found occasionally in hogs.

The pork tapeworm requires an intermediate host for development. The ovum, usually discharged from an infected human being, contaminates the food or water ingested by a hog The freed oncosphere penetrates the intestinal wall of the hog *and develops into a cysticercus in its tissues*

Growth is rapid in the tissues of the hog and in 9 to 10 weeks the parasite is a fully developed infective worm now termed *Cysticercus cellulosae* The mature cysticercus is an ellipsoidal, translucent cyst, 10 by 5 mm , equipped with suckers and hooks If man eats this infected pork, called measly pork, the cysticercus is dissolved by the gastric juice The worm passes distally into the upper part of the small intestine, attaches itself to the intestinal wall by its evaginated scolex, and develops into an adult worm.

Occasionally man as well as other primates may act as an intermediate host, and this fact gives rise to the disease due to the larvae.

Disease Due to the Larvae of the Pork Tapeworm. Man, if he ingests the ova, may become the intermediate host for the development of *Taenia solium,* and if so, the cysticerci develop in his muscles and other tissues. This may come about by the ingestion of food or water contaminated by the ova from carriers of the adult worm, or by auto-infection through the regurgitation of ova into the stomach by reverse peristalsis In order of frequency, the larvae involve the subcutaneous tissues, brain, eyes, muscles, heart, liver, lungs and peritoneum.

irritant, infection or a foreign body inclosed in the wall of the intestine (fish bone or unabsorbed suture).

Judd expressed the belief that granulomas are often formed in adhesions to contiguous loops of bowel, the omentum, or other organs. Small abscesses and fistulous communications between loops of bowel or connecting the intestine with the body surface, urinary bladder, or vagina are common sequelae.

The causative agent, a foreign body, may frequently be found embedded deep within the lesion as a nucleus about which is a zone of inflammatory cells encircled by a thick wall of fibrous tissue.

Pain near the site of the lesion is perhaps the commonest symptom of intestinal granuloma. Chronic incomplete intestinal obstruction is often present. In many cases the long history of abdominal complaints, often intermittent in occurrence, renders the possibility of a malignant lesion remote.

Abdominal granulomas of sufficient size to produce symptoms often are associated with a palpable mass. The presence of a sinus discharging on the abdominal wall or of a mass situated immediately under a laparotomy scar should arouse a suspicion of granuloma The proctoscopic examination with biopsy will usually serve to distinguish a granuloma from a malignant lesion of the distal colon and rectum. The absence of metastasis after a mass has been known to exist for a long time often indicates a benign lesion

The feces are examined for ova and parasites. Biopsies should be made when the granulomatous lesion is accessible. The Frei antigen test is performed on all patients who have rectal lesions which are associated with stricture or granuloma.

Weber reflected that intestinal lesions of unusual roentgenologic appearance, when viewed in the light of the laboratory and clinical data, may direct one to the correct diagnosis The correct diagnosis can be established only by biopsy study The treatment is surgical.

Fecal Fistulas. Fecal fistulas occur (1) postoperatively and (2) spontaneously.

Postoperative Fecal Fistulas. Of each 10 patients who have fecal fistula which follows surgical operation, 3 will have been operated on for appendicitis. Three will have had intestinal operations for, generally, either one of two diseases: (1) regional enteritis or (2) tuberculosis Three will have had pelvic surgical intervention for either a tubo-ovarian abscess or pelvic tuberculosis, and 1 will have had an operation on the colon for diverticulitis or will have had an abscess drained which resulted from diverticulitis or chronic ulcerative colitis. There are many other causes for fecal fistulas but none so common as those just enumerated. Therefore, they are not included in this listing.

The sites of external openings of fistulous tracts, in the majority of cases, are in the right lower quadrant of the abdomen. Miscellaneous and uncommon sites are the upper part of the abdomen, posterior lumbar region, vagina, bladder and perineum. Situations of various anorectal, genitourinary and intestinal fistulas are shown in Figure 7-2, page 403.

Spontaneous Fecal Fistulas. Spontaneous [illegible] arily to abscess formation from (1) regional e[illegible] [illegible]ycosis [illegible]

[illegible] Animal Parasites. The terms helminths and vermes have been used to designate wormlike animals of three diverse phyla: (1) Platyhelminthes (flatworms), (2) Nemathelminthes (roundworms) and (3) Annelida (segmented worms). In medical parasitology all parasitic worms are collectively referred to as helminths.

Platyhelminthes (*Flatworms*). The platyhelminthes are divided into four classes of which only the Trematoda and the Cestoidea include important parasites of man.

In most instances the parasite does not evoke clinical *symptoms* other than mild chronic digestive disorders, and the presence of the worm is usually unrecognized by the patient until a segment of the worm is discovered in the feces After this discovery the symptoms are limited only by the imagination of the patient, influenced by the endless tales of folklore The most spurious symptoms are: (1) choking when hungry, the choking resulting from the worm crawling up the throat to obtain sustenance, and (2) increased hunger of the patient.

The *diagnosis* of intestinal infection depends on finding the proglottides in the feces, since the ova cannot be readily differentiated from those of *Taenia saginata*.

2. The Beef Tapeworm The life cycle of the beef tapeworm, *Taenia saginata*, is similar to that of *Taenia solium* except that the development of the cysticercus takes place in cattle instead of hogs Man is the only definitive host The cysticerci are found in cattle and have been reported infrequently from other mammals. Calves are more susceptible than older cattle. Prenatal infection in calves has been recorded The cysticercosis or larval infection has been reported in man, but in most instances identification has been somewhat uncertain.

The ova, infective when passed in the feces of man, are ingested by cattle grazing on contaminated grass On ingestion by the animal the oncospheres escape from their embryonal shell into the intestine The embryo penetrates through the intestinal wall into the lymphatics or blood vessels and reaches the intramuscular connective tissues, where it develops into a *Cysticercus bovis*. The hind limbs and hump of cattle are the selective sites, but cysticerci are also found in the heart, diaphragm, tongue and other parts of the body

When the cysticercus is ingested by man, in rare steaks or poorly cooked ground beef, it develops in the intestine into an adult worm in from 8 to 10 weeks

The adult worm causes a slight irritation of the intestinal mucosa by the mechanical action of the strobila. Usually only a single worm is present, but as many as 10 have been reported Pancreatic necrosis from the penetration of the worm into the pancreatic duct has been recorded.

Symptoms are not present until the stage is reached at which the patient observes a segment of the worm in the feces After this period there may be epigastric pain, a sinking hungry feeling, empty, gnawing sensation, and awareness of the movements of the worm. There is neither appreciable loss of weight nor increase in hunger.

The results of general examination are essentially negative. Rarely is there eosinophilia or anemia

Diagnosis is based on the recovery of the gravid proglottides or the ova in the feces. Specific diagnosis depends on the appearance of the gravid proglottis with 15 to 30 lateral uterine branches or, infrequently, on the appearance of the characteristic hookless scolex.

Prognosis is good, although it is difficult to eradicate the scolex Repeated trials by the administration of male fern, which is still the most effective vermifuge for the tapeworms, may be necessary before the scolex is obtained.

3. The Hydatid Tapeworm. Hydatid disease, hydatid cyst, is caused by *Echinococcus granulosus*, of the superfamily Taenioidea Heavy infections occur in the sheep-raising and cattle-raising districts of South America, Australia, New Zealand, South Africa, Asia, central and northern Europe, and the Mediterranean countries. Indigenous infections have occurred in North America

The definitive hosts of *Echinococcus granulosus* are dogs, wolves, jackals, coyotes and other Canidae The intermediate hosts are herbivorous animals and hogs. The larval worm is a parasite for man in regions where it is prevalent among herbivorous animals.

The ova are ingested by man and pass to the duodenum where the embryos are liberated They attach themselves by means of hooklets to the intestinal mucosa, penetrate the intestinal wall, and pass into the lymphatic or the mesenteric venous blood stream, and thus are transported to various parts of the body.

During the stage of invasion there usually are no *symptoms* unless the infection is heavy, when there may be muscular pains and mild fever.

Cerebral cysticercosis is always associated with general cysticercosis The presence of general cysticercosis is often not recognizable. Occasionally, however, cysticerci are found in the brain only. Invasion of the brain and nervous system produces grave symptoms, which do not occur until the parasite dies. On the death of the parasite the symptoms are those of intracranial hypertension, severe headaches, convulsions, epileptiform attacks and often papilledema. Contractures and motor and sensory paralyses ensue. Recurrent epileptic attacks range from petit mal with or without loss of consciousness to various stages of major epilepsy with aura. *Other cerebral manifestations* are vomiting, vertigo, muscular convulsions, hemiparesis, optic neuritis, aphasia, encephalitis, disseminated sclerosis, psychic disturbances and mental deterioration. Involvement of the spinal cord may produce hyperesthesia and altered reflexes.

Taenia solium is the commonest larval tapeworm to invade the eye, which it reaches by chance through the retinal or uveal vessels. The patient may experience infra-orbital pain, flashes of light, grotesque figures in the field of vision, and blurring and loss of vision. The cysticercus may be observed moving in the vitreous fluid.

In the eye the cysticercus, usually single and 6 to 14 mm. in size, is subretinal or in the vitreous humor, where it appears as a free or attached, elongated, light gray body The retina may be detached, the vitreous fluid slightly cloudy, the parasite surrounded by an inflammatory exudate, and the iris inflamed. Death of the parasite leads to iridocyclitis with pupillary occlusion and chemosis of the conjunctiva.

Involvement of the cardiac muscle may cause tachycardia, dyspnea, syncope and abnormal heart sounds.

On *examination* the cysticerci in the subcutaneous tissues appear as smooth, firm, oval, palpable nodules varying in size from being distinctly palpable to 1 cm. in diameter, sometimes larger. On the death of the larvae the nodules become more noticeable by an increase in fluid and an inflammatory reaction. Calcification ultimately results

In the brain cysticerci produce findings characteristic of cerebral edema, purulent meningitis, meningo-encephalitis, encephalomalacia and endarteritis. Along with or without any one or more of these manifestations may occur the topical signs and symptoms of single or multiple cortical tumors

The larvae have a peculiar affinity for the diaphragm After calcification has occurred, roentgenologic studies may reveal the presence of multiple calcified cysticerci which are accurately interpreted by the trained roentgenologist.

An eosinophilia of 5 to 12 per cent, but occasionally considerably higher, is a fairly constant but not invariable finding in cysticercosis. The feces do not contain the characteristic ova unless the cysticercosis is an instance of auto-infection

The *diagnosis* of cysticercosis is established by a biopsy of a palpable subcutaneous nodule A history of intestinal taeniasis and the presence of multiple nodules and a moderate eosinophilia are suggestive In cysticercosis of the brain and internal viscera, diagnosis is established by clinical symptoms, in the brain, perhaps by ventriculograms.

The prognosis for cysticercal infection depends on the location of the larvae. If the infection is limited to the muscles and subcutaneous tissues, the *prognosis* is favorable even with heavy infections, since the nodules in time become calcified; but if the cysticerci are present in the brain, heart or important viscera, the prognosis is grave.

Disease Due to the Adult Pork Tapeworm. The adult worm, usually a single [illegible] other than slight local [illegible] and the attachment of the scolex.

(wall-eyed pike), *Stizostedion canadense griseum* (sand pike), and *Lota maculosa* (burbot), have been found to harbor the parasite In Long Lake, Ely, Minnesota, the wall-eyed pike average 6 larvae and pickerel, 15 larvae These fish also harbor the larvae of other species of *Diphyllobothrium* that may be mistaken for *Diphyllobothrium latum*

The adult worm may produce a catarrhal condition of the intestinal mucosa Usually infection is limited to a single worm, although more may be present. *Tapeworm anemia* is more prevalent in women than in men and is most frequently observed in the spring and summer

Belding has summarized the various opinions regarding the origin of this anemia which have been advanced (1) The tapeworm is the direct cause of the anemia (2) It is a precipitating factor for an existing constitutional predisposition. (3) A true pernicious anemia may simultaneously occur in an infected individual.

There is no good evidence of a specific hematoxin created by this worm. Abortive forms of pernicious anemia can occur among patients affected. In fact, other intestinal worms at times are capable of producing a similar type of anemia.

Most persons suffer no ill effects from the fish tapeworm In a small percentage of infected persons there develops a severe *Dibothriocephalus* anemia that often hematologically resembles pernicious anemia In such instances there are the pallor, weakness, dyspnea and other symptoms characteristic of severe anemia from any cause

Unless there is evidence of an anemia present, the findings on general examination are not remarkable In those who have an anemia, the erythrocyte count varies from 1,500,000 to 3,000,000 per cubic millimeter of blood, the hemoglobin may be as low as 25 to 30 per cent The color index remains above unity (see Chapter 12). There is a leukopenia and usually, but not invariably, a more or less pronounced eosinophilia Achlorhydria is present in four fifths of these patients, and paresthesia may develop

The diagnosis is based on finding the characteristic operculate ova or the evacuated proglottides in the feces In a few instances a correct diagnosis may be suspected if the patient resides in an endemic locality, eats raw fish, and has a pernicious type of anemia

It has been common in some medical schools to ask a hypothetic question: "A fat Finnish woman, a cook by trade, has ... wer. "Fish tapeworm anemia" Jews, Russiar ... om- monly infected, and women, as stated, more frequently than men, possibly because of nibbling raw fish when preparing meals

The severest grades of anemia clear up after the successful administration of the male fern

Nemathelminthes (*Roundworms*) The Nemathelminthes of medical importance include three classes class 1, Nematoda, class 2, Nematomorpha; and class 3, Acanthocephala

Class 1 The Nematoda The nematodes are classified as belonging to the phylum Nemathelminthes that have an intestinal tract These are common but often transient parasites of man

The intestinal nematodes may maintain their positions and obtain their nutrition by temporary attachment or retention in the folds of the mucosa and by feeding on the intestinal contents (*Ascaris*) By means of an oral attachment to the intestinal mucosa some (*Ancylostoma*) may live by biting with their oral structures and ingesting blood. Some may live by anchorage with their attenuated ends and thus cause lysis of tissues for purposes of nutrition (*Trichuris*) There are those that penetrate the tissues of the intestines for nutriment Finally some (filarial worms) penetrate to the interior of the body and depend on the absorption of nourishment from the body fluid

The parasitic nematodes vary in their ability to produce mechanical ... and most of all in their ability to select ... which may be required to produce dise

Of the hydatid cysts the unilocular cysts are the common ones present in man They require several years for development. Those of great size, about 6 to 8 inches (15.2 to 20.3 cm) in diameter contain the so-called daughter cysts. Daughter cysts may arise from the germinal membrane, the brood capsules, or the scolices.

The liver is the chief site of hydatid cysts, and since the right lobe of the liver is the largest part of the organ, the most hydatid cysts will be found there. The lungs, abdominal cavity, muscles and subcutaneous tissues, kidneys, spleen and bones are often invaded, while cysts are less frequently found in the pleura, heart, brain, spinal cord, orbit and other regions

Rupture of hydatid cysts sets free scolices, bits of germinal membrane, brood capsules and daughter cysts which may reach other tissues through the blood or by direct extension and develop into secondary cysts Hepatic cysts may also rupture into the abdominal cavity, the gallbladder, biliary ducts or through the diaphragm into the pleural cavity

A hydatid cystic form termed alveolar cyst is neoplastic; it gives rise to metatasis in other organs by direct extension or through the lymphatics or the blood stream Opinions differ in regard to the origin of this cyst. The mechanism of its production is not known. An alveolar cyst has the appearance of a porous spongy mass of small irregular cavities or vesicles separated from each other by connective tissue. The alveolar hydatid is usually sterile but occasionally it contains brood capsules and scolices Calcification is often present

The osseous cysts have no regular adventitia

Infection is usually acquired during childhood, but unless the brain or the orbit is infected, symptoms do not usually appear until later in life. Most of the cases in the United States are traceable to the association with dogs, and usually the patient is of Mediterranean stock

The symptoms are those produced by a slowly growing tumor, arising in the same situation as the hydatid cyst. These symptoms are considered, in this text, with diseases of the organs in which hydatids occur.

A slight eosinophilia is present in about one half of the infected individuals. General eosinophilia occurs when there is seepage of the cystic contents. The eosinophils neutralize the toxic products of protein degradation and are essential cellular elements in hydatid allergy Precipitative and complement-fixing antibodies have been demonstrated in the blood and spinal fluid.

Clinical diagnosis is based on the presence of cystic tumors. Roentgenologic examinations are particularly useful in diagnosis and in locating cysts.

Diagnosis depends on finding the scolices, brood capsules or daughter cysts in the hydatid fluid. The exploratory puncture for the purpose of obtaining fluid is contraindicated as a dangerous diagnostic procedure since leakage may cause secondary echinococcosis and anaphylactic shock Precipitative, complement-fixation and intracutaneous tests have been used with more or less success.

The prognosis is good when the primary cyst is accessible to surgical removal.

Fish Tapeworm Infection The Superfamily Bothriocephaloidea. The cestodes of the superfamily Bothriocephaloidea, order Pseudophyllidea, that are parasites of man belong to the family Diphyllobothriidae, the members of which inhabit the intestines of mammals, birds and reptiles

Diphyllobothrium latum (*Bothriocephalus latus*, or *Dibothriocephalus latus*) causes fish tapeworm infection, known also as diphyllobothriasis, bothriocephaliasis, *Dibothriocephalus* anemia, or broad-tapeworm infection

In North America the worm has been introduced into the Great Lakes region by [illegible] There are three principal endemic areas: ([illegible] northern Minnesota and (3) the vicinity o [illegible]

The life cycle [illegible] involves two intermediate hosts, copepods and fresh-water fis[illegible] *[illegible]ostedion vitreum*

In North America four sp[illegible]

The specific invasion of the muscles is characterized by muscle stiffness, jelling and pain. *In severe infections the muscle pain and tenderness, fever, edema, cachexia* and prostration are extreme.

Symptoms occasioned by the involvement of the central nervous system are those of encephalitis: drowsiness, headache, nausea and vomiting, fever, mental confusion, disorientation, apathy, stupor, delirium, paralysis, muscular hypotonicity, diminished deep reflexes and coma. The pulmonary symptoms are those of pulmonary edema.

Death may occur when infection is intense or when resistance is low because of pre-existent weakness in vital organs In overwhelming infections it may take place *in the second or third week but more often it occurs from the fourth to the eighth* week from exhaustion, pneumonia or cardiac failure In epidemics the mortality rate may be as high as 1 death in each 3 cases of the infection.

On examination there are present a chemosis of the bulbar conjunctiva and changes in the periphery of the retina Encapsulation of larvae in the ocular muscles often takes place and there may be soreness on bulbar pressure and movements of the eyes. There are profuse sweating, rapid cardiac and respiratory rates, edema of the face, and often urticaria General muscular soreness and rheumatic pains with an inability to use the involved muscles are present, as are a feeble or a dicrotic pulse, muffled cardiac sounds, an apical systolic murmur, and palpitation. The electrocardiogram reveals evidence of myocardial damage.

The leukocyte count may range from normal to 30,000 per cubic millimeter. Eosinophilia, which appears about the fourteenth day, is a characteristic finding It ordinarily runs from 15 to 50 per cent, but may be about 75 per cent. The eosinophilia is not correlated with the severity of the disease. The eosinophilia may be low when there is a concomitant bacterial infection. It persists, for a 2 to 7 per cent eosinophilia has been found from 4 to 7 years after the disappearance of clinical symptoms Humoral immunity is evidenced by the production of precipitative and complement-fixing antibodies

Clinical diagnosis is established by the history of eating pork, the existence usually of more than one case of the disease, eosinophilia and myositis. The myositis and the demonstration of the parasites by performance of biopsy of muscle are diagnostic. The biceps, deltoid or gastrocnemius muscles are used for biopsy.

The several methods of laboratory diagnosis include (1) examination of the blood for eosinophilia, (2) the detection of adult worms in the feces and of larvae in the blood and spinal fluid and (3) the biopsy of muscles for encysted larvae.

If the patient survives for a month, recovery usually slowly ensues

2. *Trichuris trichiura.* This is one of the two species of the genus *Trichuris,* of the family Trichuridae, which are parasitic to man *Capillaria hepatica* is the other species of the worm which is parasitic

Trichuris trichiura causes *whipworm infection* The parasite maintains its position by embedding the anterior portion of its whiplike structure in the intestinal tissues of the host

The symptoms are not definite

Diagnosis is made by finding the characteristic barrel-shaped ova in the feces The worm is difficult to eradicate Prognosis is good as far as the health is concerned.

3 *Strongyloides stercoralis* Of the family Strongyloididae, superfamily Rhabditoidea, *Strongyloides stercoralis* is pathogenic for man, and causes the infection *strongyloidiasis*

Man acquires the infection usually from the soil

The infective filariform larvae penetrate the skin of the mammalian host, enter the venous circulation and pass through the right side of the heart to the lungs, *penetrate* the capillary walls into the alveoli, and ascend to the glottis, are swallowed, and reach the upper part of the intestine. By this time the worms are nearing maturity and thus they develop into adults in a short time Mature females ready for oviposition are pro-

number may overcome the resistance of any host. The local reactions are induced by both physical and chemical irritation. The reactions to these irritants comprise inflammation, necrosis, repair and encapsulation as a result of tissue sensitization and foreign body response. General reactions occur from an allergic response to foreign proteins, and indirectly from injury to vital organs.

In some individuals there is a supersensitiveness to infection which seems to be best accounted for by assuming it to be a phase of immunity that represents the reaction of the host against the proteinic products of the parasitic nematode. Supersensitiveness is manifested by both local and general reactions. Supersensitiveness may be demonstrated by cutaneous tests with antigens derived from the parasites and their products In some nematodes such diagnostic tests represent group reactions for allied species.

1. *Trichinella spiralis.* This nematode is of the family Trichinellidae, superfamily Trichuroidea The adult worms inhabit the intestine, and the larvae the muscles, of mammals and cause the disease *trichinosis.*

Trichinosis is prevalent where pork is eaten raw or insufficiently cooked, for in order to complete the life cycle of the parasite, flesh containing the encysted larvae must be ingested by another host Trichinosis occurs in Europe and in the United States of America, but is rare in Africa and South America

The incidence seems to be higher in the North Atlantic States than in other sections of the United States Trichinosis shows seasonal fluctuations, reaching its peak during the winter months when there is greater consumption of pork. In some instances, when summer sausage is ingested, epidemics of trichinosis may occur. Everywhere the disease is most frequently diagnosed or observed at necropsy.

When infected larvae are ingested by man, they pass to the small intestine where the capsules are dissolved and the larvae released The young larvae attach themselves to or invade the intestinal mucosa Within 2 days the worms reach sexual maturity and mate. After fertilization the female burrows into the mucosa of the intestinal villi and in 6 days deposits successive broods of larvae into the lymph spaces. Occasionally larvae may be liberated into the intestine.

From the lymph spaces the larvae enter the blood stream and are carried to all parts of the body.

The larvae select the tendinous portions of the muscle and soon each larva is enclosed in a capsule The processes of formation of an encapsulated larva comprise a focal acute inflammation in the muscle and degenerative changes. As a climax to many of the degenerative changes is calcification, which may begin as early as 6 months but requires months if not years for completion

During the period of larval migration the myocardium may show focal areas of interstitial cellular infiltration and at times fragmentation of the muscle fibers, fatty degeneration and necrosis.

The larvae have been found in the spinal fluid and the brain The changes in the brain are generalized hyperemia, perivascular infiltration, especially in the cortex, and granulomatous nodules around the parasite These nodules are most numerous in the basal ganglia, medulla and cerebellum.

The larvae may invade the lungs, pleura, pancreas, gallbladder, kidneys, and other organs, producing local inflammation and edema. There may be hyperplasia of bone marrow and increase of eosinophils.

The symptoms are associated with the activities of the parasites which are in- [illegible] and adult worms [illegible]

varying degrees of respiratory, ocular, and cardiac symptoms develop, and occasionally, when the fever is high, a maculopapular erythema is apparent. These symptoms may persist, characterized by fluctuation, from one to two weeks

skin. Within the body the larvae enter the blood, reach the lungs, ascend to the pharynx and pass down to the intestine where they become adults

Infection may be had by acquiring the larvae through drinking water or contaminated food.

The pathologic changes of hookworm infection comprise these in the skin at the site of entry, in the lungs, and in the small intestine, the habitat of the adult worm

There is a papulovesicular, pustular eruption at the point of penetration of the skin by the larvae.

As the migrating larvae pass into the alveolar spaces from the pulmonary capillaries, they cause petechial hemorrhages, and in heavy infections the inflammatory reaction may be so extensive and so severe as to produce a lobular pneumonia, particularly if accompanied by the secondary bacterial infection

The adult worms adhere to the intestinal mucosa with their buccal capsules, sucking blood and tearing off bits of mucosa Secondary bacterial invasion may lead to the formation of small ulcers at these sites The continuous loss of blood is the chief cause of hookworm anemia

Ground itch or hookworm dermatitis is caused by the larvae. The acute itching edematous erythema is followed by a papulovesicular eruption that may become pustular and ulcerative from pyogenic infection and may persist for weeks. Sensitive persons sometimes show urticaria

At times massive infections induce acute symptoms consisting of severe abdominal pain, sudden loss of strength, prostration, and circulatory and pulmonary disturbances. Infections with *Ancylostoma duodenale* are more serious and produce symptoms with fewer worms than infections with *Necator americanus*

Absence of symptoms occurs in those who have good health and mild infections Patients who have mild symptoms usually evidence vague dyspepsia and weakness (laziness) In more intense infections there is diarrhea with mucus and blood As a part of the anemia, there are palpitation, dyspnea and mental and physical depression The patient is listless, with apathetic puffy face and flabby muscles, and may show paresthesia, mental apathy and sexual dysfunction In severe and often fatal infections there are profound anemia, edema often with ascites, diarrhea, mental disturbances and cardiac decompensation

Infected children show physical, mental and sexual retardation Children who have fewer than 25 worms show no symptoms, with 26 to 100 a slight reduction in hemoglobin and slight mental retardation, and with more than 100, definite symptoms, namely, stunted growth, delayed sexual development, severe anemia and noticeable mental retardation

The most prominent characteristic in hookworm disease is a diminution of hemoglobin and erythrocytes The anemia begins 10 to 20 weeks after infection and is progressive It is more marked in *Ancylostoma duodenale* than in *Necator americanus* infections The erythrocytes range from 1,000,000 to 3,500,000 per cubic millimeter of blood There is a low mean corpuscular volume, a low hemoglobin and a normal or subnormal reticulocyte count. At times the blood findings are those of a macrocytic anemia

Hookworm anemia is due to the loss of blood since it may be cured by diet and iron therapy while the patient still harbors the parasites

The leukocyte count is usually from 5,200 to 10,000 per cubic millimeter, but in early infections may reach 17,000 Eosinophilia is irregular The percentage is usually from 2 to 15 per cent but during the early stages it may be as high as 55 per cent Blood cholestrol, serum protein and serum calcium are low and the glucose tolerance curve is flattened, indicating delayed absorption

Diagnosis depends on finding the characteristic ova in the feces.

Prognosis is good, except for patients in the terminal stages of the disease or those who have serious secondary complications. Recovery usually follows improved nutrition, iron therapy and administration of anthelmintics

duced in 17 or more days after the initial infection. Some of the larvae may remain in the alveolar tissues, reach adolescence in the bronchial epithelium and produce offspring that may attain the filariform stage.

An infection of the lungs and cystic duct by *Strongyloides stercoralis* is often indicative of an internal hyperinfection. Hyperinfection is brought about by the larvae developing to the filariform stage in the intestines and the skin of the perianal region and thus establishing a developmental cycle within the host.

At the site of penetration of the skin of the feet by the parasites there is intense itching. A rise of temperature, vague feelings of malaise, a slight headache and at times urticaria may ensue The migration of the larvae through the lungs may cause a febrile attack, malaise, anorexia, cough and other signs of bronchitis or sometimes symptoms of bronchopneumonia

Light infections cause no intestinal symptoms. Moderate to severe infections produce a diarrhea The general condition of the patient is usually not materially affected Prolonged infection may cause emaciation, weakness, and quick fatigue. The anemia if present is relatively slight

The general examination reveals no characteristic findings If there is a heavy pulmonary infection by the larvae, there may be the signs of bronchitis or bronchopneumonia Leukocytosis may be present during the acute infection, particularly if the lungs are involved However, as the disease becomes chronic, only a relative lymphocytosis persists Eosinophilia is usually from 10 per cent upward and at times may reach 50 per cent or more

The diagnosis depends on finding the ova in the feces. During purgation or severe dysentery embryonate ova may appear in the feces. Occasionally the ova and larvae may be found in the sputum

The prognosis is favorable except in severe cases involving hyperinfection Eradication of the worms may be difficult No known treatment is entirely satisfactory

4 *Heterodera radicicola* This nematode once was erroneously thought to be a human parasite At that time it was called *Oxyuris incognita* (family Ascaridae) because the ova were found in the feces of man, when no worms could be found Later these ova were identified as those of *Heterodera radicicola* that passed uninjured through the human intestine *Heterodera radicicola* is a parasite of the roots and stems of radishes, celery, turnips and other edible plants

5 Hookworms The species of hookworms which infest man belong to three families, Ancylostomatidae, Strongylidae and Syngamidae of the superfamily Strongyloidea

The members of the family Ancylostomatidae are parasites of the intestinal tract of mammals, and at least two species produce serious disease in man, namely, (1) *Ancylostoma duodenale* and (2) *Necator americanus* (*Uncinaria americana, Ancylostoma americanum*) Another species, *Ancylostoma braziliense*, is well known for its ability to produce ground itch, but it is incapable of producing intestinal disease in man.

The distribution of these species has been brought about by the migration of peoples *Necator americanus* is said to have been brought here by Negro slaves and immigrants, and similarly *Ancylostoma duodenale* was spread throughout the East by Chinese colonists.

The present geographic distribution of the hookworm extends in the tropical and subtropical zones between latitudes 45 degrees N and 30 degrees S, except for the presence of *Ancylostoma duodenale* in the more northerly mining districts of Europe *Necator americanus* is the prevailing species in the Western Hemisphere

Ancylostoma braziliense is a parasite of domestic and wild feline and canine animals in the tropics and subtropics It is present in Brazil and the Southern United States

The ova of all hookworms are passed in the feces, and hatch in the soil. The rhabditiform larvae grow rapidly and molt into infective filariform larvae that penetrate the

skin. Within the body the larvae enter the blood, reach the lungs, ascend to the pharynx and pass down to the intestine where they become adults.

Infection may be had by acquiring the larvae through drinking water or contaminated food

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Prognosis is good, except for patients in the terminal stages of the disease or those who have serious secondary complications Recovery usually follows improved nutrition, iron therapy and administration of anthelmintics

6. *Ascaris lumbricoides.* This worm, of the family Ascaridae, of the superfamily Ascaroidea, infects hogs, mice, rats, rabbits and man, causing the disease *ascariasis*, a common infection.

Ingested ova hatch in the duodenum. The larvae traverse the intestinal wall until they reach the lymphatic vessels or the venules, pass to the liver, thence by the hepatic veins to the heart and ultimately to the lungs

In the lungs the larvae penetrate the capillaries to enter the alveoli Occasionally some return to the left heart through the pulmonary veins and are distributed as emboli in various parts of the body. In the lungs the growing larvae molt twice, on the fifth to sixth day and on the tenth day They migrate to the bronchi, ascend the trachea to the glottis, and pass down the esophagus, eventually reaching the intestine

The normal habitat of the adult worms is the small intestine. Their attachment to the mucosa is temporary since they are capable of moving

In the lungs the larvae set up an inflammatory process with numerous petechial hemorrhages at the site of entrance into the alveoli In severe infections there may be a lobular pneumonia.

In heavy infections intestinal obstruction with gangrene and intussusception has resulted from masses of worms

Invasion of the gallbladder and biliary tracts produces chronic irritation and inflammation of the gallbladder and obstruction of the common duct, with jaundice, pain and other symptoms of gallbladder disease

Ectopic infections have caused iritis from intra-ocular invasion by the larvae, and middle-ear disease, and ascarids have been found in the right ventricle of the heart.

Except in the presence of heavy infections there are no symptoms

The symptoms occurring during larval migration are headache, urticarial skin lesions, fever, muscular pains, coughs, dyspnea, hemoptysis and hepatic enlargement Bronchopneumonia, often fatal, occurs among children in highly endemic regions Repeated infections tend to maintain a chronic type of pulmonary infection

The commonest complaint arising from the presence of the adult worm is general abdominal discomfort with nausea, colicky pains, abnormal digestive disturbances, and loss of appetite Reflex nervous symptoms, common in young children, include irritability, colicky abdominal pains, disturbed sleep, picking at nose, grinding of teeth, and occasionally convulsions. Symptoms simulating epilepsy and meningitis have disappeared and night blindness has been cured after the removal of the worms.

Supersensitiveness may be acquired by contact and does not necessarily predicate previous infection

Examination of a patient otherwise healthy and well nourished does not reveal any findings characteristic of *Ascaris* infection In severe infections in children and debilitated starved adults there are weakness and anemia Eosinophils may reach 7 to 10 per cent of the leukocyte count

During migration of the larvae abscesses may be present in the muscles or subcutaneous tissues Bronchitis or bronchial pneumonia, hepatitis and jaundice may be found An acute hemorrhagic nephritis may be suggested by the urinary findings Abscesses of the middle ear due to the larvae may be present.

Occasionally the adult worms are passed in the feces or are regurgitated A definite diagnosis is established by finding the ova or the adult worm in the feces or in the vomitus. At times only male worms are present, hence no ova can be demonstrated In such cases diagnosis must be based on finding the adult worms. Intracutaneous and precipitative diagnostic tests are not practical

As a rule, prognosis is favorable.

Intestinal Myiasis. Intestinal myiasis in man is largely accidental, although some 30 species of dipterous larvae have been found in the digestive tract These accidental invaders are from flies that breed in decaying organic matter. The intestine, however, is the normal environment of the parasitic *Gasterophilus* larvae The larvae of the flesh flies of the genus *Sarcophaga* may gain entrance through the

anus when the eggs are deposited at the anal orifice of infants. Many larvae are destroyed by the digestive juices, but others are able to live in the intestinal tract and may produce intestinal distress (see Chapter 20).

Giardiasis or Lambliasis. *Giardia lamblia* of the family Hexamitidae resides in the proximal segments of the small intestines from the duodenum downward and in the bile ducts. This flagellate, commonly called also *Giardia intestinalis* and *Lamblia intestinalis,* is the cause of the disease *giardiasis* or *lambliasis.*

The symptoms are vague Most infected persons do not have symptoms. Those symptoms ascribed to giardial infections in adults include anorexia, headache, epigastric pain, irregular bowel movements, alternating diarrhea and constipation, nutritional disturbances, neurasthenia, anemia and fatigability. Hartman has expressed the belief that *Giardia* may give symptoms comparable to those of biliary disease and even approximate the typical syndrome of chronic cholecystitis Infections in children produce various effects, ranging from no symptoms to those of enteritis A "giardial syndrome" consisting of protracted diarrhea, gradual distention of the abdomen and retardation in growth has been described, and constipation, nervousness, fatigue and loss of appetite have been reported

Giardial infection is diagnosed by finding the cysts or occasionally the trophozoites in the feces The latter are more readily obtained by duodenal drainage, which is the most reliable method of diagnosis The distinctive structure of both trophozoite and cyst readily distinguishes *Giardia lamblia* from other intestinal flagellates.

Isospora hominis (*Coccidium hominis*) *Isospora hominis,* a species of coccidia, causes the disease termed human coccidiosis, a rare and poorly understood disorder. The pathogenicity of the organism is not definite

The oocysts which are found in the stools are probably ingested as such in food and drink, and since closely allied coccidia are found in many animals, these creatures doubtless serve as a reservoir

Diseases Due to Static or Mechanical Abnormality. ***Intestinal Obstruction.*** The term ileus is used as a synonym for intestinal obstruction When modified by the word *dynamic,* it indicates a mechanical obstruction; if by *adynamic, paralytic,* or inhibition, it denotes the absence of peristaltic activity

The incidence of the various forms of intestinal obstruction is not known Obstruction from intussusception is the commonest form in childhood Obstruction from adhesions is seen at all ages but particularly in early adult life External hernia as a cause of obstruction is also encountered in all age groups but is commonest in late middle life Old age is the period at which obstruction often is caused by carcinoma and vascular accidents such as mesenteric thrombosis.

There are forms of intestinal obstruction which often can be suspected or diagnosed prior to surgical intervention or postmortem examination

Obturation Obstruction. Sudden occlusion of the lumen of the intestine by a foreign body is a relatively rare type of ileus which is termed obturation obstruction. Obstruction of the intestinal lumen by a gallstone or by a foreign body of any kind is an example of this type of mechanical intestinal obstruction. Gallstones usually reach the bowel by passing through a fistula The commonest site of fistulization is between the gallbladder and the duodenum, or the gallbladder and the ileum Half of the stones that enter the intestine are carried along and passed spontaneously with a bowel movement

The symptoms which a gallstone or a foreign body may produce after entering the bowel depend on the size of the object and the presence of abnormalities in the bowel. In the normal intestine the commonest site of obstruction by a gallstone or

change as it passes distalward in the intestine. In some instances there are constantly present the symptoms of intestinal obstruction, beginning in the proximal portion of the intestine and shifting distally as time passes.

The variations in the symptoms in obturation ileus and the somewhat prolonged low-grade distress present prior to the development of complete obstruction contribute to the difficulty of diagnosis unless the gallstone or the foreign body can be detected by roentgenologic examination. The history in obturation ileus of swallowing an object may or may not be helpful. It is important to know that gallstone obstruction may occur in a patient who has no history of gallbladder disease or colics.

Intussusception. Intussusception is the invagination of one part of the intestine into the lumen of another part Such an occurrence is often associated with the phenomena of intestinal obstruction. Intussusception is a disease primarily of childhood, although it does occur in adults The common site for intussusception is about the ileocecal valve It may occur, however. in the ileocecal, ileocolic, enteric, and colic segments

Intestinal tumors, ulcerations, or diverticula may be present at the apex of the intussusception in adults Since most intussusceptions occur in early life in those who have no intestinal disease, primary intussusceptions are often ascribed to some such cause as an irregular action of the intestinal musculature and increased peristalsis

The injury which follows from intussusception is largely limited to the intussusceptum as the result of compression by the contractions of the intussuscipiens and by interference with its blood supply Engorgement and edema permit passage of blood and mucus into the lumen Ulceration of the intestinal wall and, as a consequence of strangulation, gangrene may ensue The gangrene often permits a slough of the prolapsed segment of the intestine A complete obstruction of the bowel often is not present in intussusception

If an intussusception is cut along its longitudinal axis to its lumen and the cut surface is viewed laterally, it is seen to consist of parallel layers consisting of the full thickness of the wall of the intestine (exemplified in a partially invaginated finger of a glove). arranged so that mucous membrane is in contact with mucous membrane and peritoneum with peritoneum The outermost layer forms the *intussuscipiens* The middle and the innermost layers comprise the *intussusceptum*, the innermost layers are the entering portion The apex of the intussusception is formed by the junction of the entering and returning layers

Symptoms Intussusception occurs either in an acute or in a chronic form The acute intussusception is common in childhood In acute intussusception abdominal pain, vomiting and the passage of blood and mucus by bowel are common symptoms Pain is sudden in its onset and occurs in paroxysms The intervals between paroxysms of pain may vary from a few minutes to a few hours in duration During these intervals there is often complete comfort There is a tendency for the pain to become somewhat less severe after the intussusception is completed

Vomiting is not a constant symptom of intussusception If present, vomiting may give temporary relief of pain

In the majority of cases of acute and subacute intussusception there is some diarrhea at first and then absolute constipation The passage of blood and mucus is rarely profuse Bloody mucus may not be passed, it may be found in the rectum on examination

Tenesmus is more commonly seen in the acute extensive ileocecal forms of intussusception than in other forms

A chronic intussusception may cause symptoms of partial intestinal obstruction or it may be present without symptoms

Examination. The significant finding on examination of the abdomen is an abdominal mass In more than half of these patients a mass can be felt on bimanual examination of the pelvis The situation of the mass is dependent on the origin and

growth of the intussusception. The intussusception may eventually reach the anus and even project from it

DIAGNOSIS The diagnosis of acute intussusception often can be made from the history and the examination. Assistance can be obtained from the use of the roentgenogram, though the barium enema may correct the defect and barium should not be administered by mouth

An acute intussusception may be simulated by simple enterocolitis, appendicitis, mesenteric thrombosis and Henoch's purpura

Prognosis depends on the treatment, which is surgical.

The mortality rate of operative reduction of intussusception is usually less than 10 per cent in patients operated on within 12 hours after the onset A mortality of more than one half occurs among patients undergoing operation later than 72 hours after the onset

The nonoperative reduction of intussusception has enthusiastic advocates The recurrences of intestinal intussusception usually are the result of some local intestinal abnormality such as polyp or diverticulum which should be surgically removed.

Volvulus. *Volvulus is an intestinal obstruction which results from a cordage* maneuver (twisting) of the bowel, often about its mesenteric axis. The directions and progression pursued by the intestine in accomplishing the twist are unknown Volvulus as a cause of intestinal obstruction occurs in about 1 of every 8 patients less than 20 years of age who have intestinal obstruction

The segments of the bowel most commonly performing volvulus are, first, the small intestine and, second, the sigmoid flexure (see Anomalies of Fixation, p 929).

Volvulus and Strangulation. Arterial obliteration occurs in volvulus but in its most exquisite form it is observed in mesenteric thrombosis or embolism. When the artery is occluded, hemorrhagic necrosis follows and plasma is lost by extravasation into the peritoneal cavity. When a medium sized vein is occluded bleeding occurs into the lumen of the intestine and blood, in large quantities, is passed in the fecal movements.

In strangulation both arterial and venous occlusion occur and there is a loss of whole blood into the wall and lumen of the bowel This loss of blood may be sufficient to account for profound shock and, in an occasional instance, death

Death may result from strangulation, gangrene, rupture of an obstructed bowel, or from the passage of infecting organisms through a devitalized intestinal wall. In high uncomplicated obstruction the resulting dehydration and disturbance of the normal chemical balances of the blood and the effects of these on the functions of various organs, notably the kidneys, may cause death (see Abdominal Apoplexy, p. 895).

Manifestations of Intestinal Obstruction. In obstruction in the proximal segments of the small intestine, vomiting is always a common symptom. When the obstruction is in the distal segments of the small intestine, vomiting is irregular and less intense In obstruction of the distal part of the small intestine, the vomitus contains colon bacilli, which impart to it a fecal odor (fecal vomiting).

As the result of the vomiting or the loss of fluid removed by nasal suction, when the obstruction occurs in the proximal part (high) of the small intestine, there ensue dehydration and alteration in the composition of the blood There is a decrease in chloride and sodium ions, and a rise in nonprotein nitrogen. Depending on the proportions of gastric juice and bile and pancreatic juice lost by vomiting, either acidosis or alkalosis may follow

When obstruction is present in the lower part of the small intestine, vomiting cannot empty the bowel Fluid and air accumulate and distention of the bowel is the prominent feature If obstruction occurs within the colon, *the tendency to distention*

pour into the colon but preventing regurgitation from the colon into the small [in]testine In this way a closed-loop type of obstruction is produced, distention be[co]mes extreme and a grave emergency *ensues requiring surgical operation.*

Reverse peristalsis and vomiting protect the intestine from the ill effects of [dis]tention Reverse peristalsis and vomiting are ineffective protective mechanisms [in t]he presence of closed-loop types of intestinal obstruction.

The local symptoms of obstruction are abdominal pain, vomiting and obstipa[tio]n. Pain is always present in an early mechanical obstruction. The pain is a true [col]ic in nonstrangulated obstruction and occurs in waves There is a free interval [bet]ween the periods of pain The pain is situated in the central part of the abdomen [wh]en the obstruction is *in the small intestine, and below the level of the umbilicus* [wh]en in the colon With each period of pain the patient is aware of the increased [per]istaltic activity and frequently feels and hears the movement of fluid and gas in [the] abdomen As distention becomes pronounced, or when the onset of strangulation [occ]urs, the discomfort becomes constant and it may be severe.

Complete obstipation is considered to be characteristic of obstruction. Complete [obs]tipation is defined as an inability to pass feces or gas after the initial enema and [a st]atement by the patient that no gas has been expelled since the enema.

EXAMINATION Evidence of increased peristaltic activity may be obtained by both [ins]pection and auscultation. Distention is more pronounced with low than with high [obs]truction and increases with the duration of the process. In high obstruction, if [vom]iting has emptied the gut, distention is absent.

Ability to hear increased peristalsis is the rule. In the normal abdomen, peristalsis [is a]udible and peristaltic rushes can often be heard. Auscultation of the abdomen [yield]s valuable information concerning the presence or the absence of intestinal [obs]truction; but only to those who have listened to a sufficient number of normal [abd]omens to evaluate what is heard in intestinal obstruction. The characteristic of [the] borborygmi heard in obstruction is their accentuated timbre during the waves of [pai]n which the patient experiences The absence of audible peristalsis is a character[isti]c feature of paralytic ileus, which is frequently a result of peritonitis

Palpation of the abdomen may yield completely negative findings in proximal [and] uncomplicated obstruction Tenderness, when present, may be of some localiz[ing] value concerning the situation of the obstruction. Palpation often gives assistance [in d]etecting the presence of intussusception, particularly in early childhood, by [feel]ing a small mass at the site of the lesion In general, palpation of a mass in the [adu]lt abdomen is not successful unless a very large tumor is present.

At the onset and after strangulation is present, the patient evinces a greater sense [of p]rostration and shock and appears much more ill than the duration of the obstruc[tion] seems to warrant Tachycardia and low blood pressure are usual

The proper interpretation of a plain posterior-anterior roentgenogram revealing [the] presence or the absence of distended loops of the intestines and their luminal [top]ography, as well as their situation in the abdomen is a most valuable examination [in i]ntestinal obstruction.

In many cases of distal intestinal obstruction the blood count remains normal. [An] increased leukocyte count is important as an indication of the presence of pos[sibl]e strangulation or leakage, and when there is an increase in the leukocyte count [wit]hout evidence of hemoconcentration, it is suggestive that strangulation has [dev]eloped.

In some instances of proximal intestinal obstruction the pronounced dehydration [du]e to *vomiting* may cause sufficient hemoconcentration to produce an elevation in [the] hemoglobin value and in both the erythrocyte and the leukocyte counts A

parallel rise in all of these values suggests that a concentration of the blood has taken place.

Changes in the blood chloride and urea nitrogen and, to a lesser degree, in the carbon dioxide combining power and the proteins of the blood, are due to the influence of the dehydration and plasma loss that occur during the course of obstruction. The determination of the concentration of these elements in the blood is of assistance in measuring the chemical imbalance. It is of no help in the diagnosis of obstruction.

DIAGNOSIS The diagnosis of acute mechanical intestinal obstruction may be obvious from the presence of cramping intermittent pain, followed by vomitus containing intestinal contents, and obstipation. In the presence of obesity, ascites and distention the plain posterior-anterior roentgenogram of the abdomen may be conclusively positive.

In many instances the finding on examination of a definite cause for one or the other type of intestinal obstruction, for instance an incarcerated hernia in mechanical obstruction, or evidence of peritonitis for a paralytic ileus, is diagnostically important.

Intestinal Obstruction Due to Disturbance of Innervation or of Psychic Control (*Paralytic Ileus and Spastic Ileus*). Paralytic ileus is due to infection or to a disturbance of innervation Spastic ileus is due to a lack of psychic control.

Paralytic Ileus Adynamic or paralytic ileus is the commonest form of intestinal obstruction and is caused usually by a general peritonitis. Intestinal function and motility cease. Paralytic ileus occurs often after abdominal operation It may commence during the course of pneumonia, empyema and septicemia Traumatic wounds, hemorrhage, spinal cord injuries, and broken bones may be attended by paralytic ileus The extravasation of blood, perforated peptic ulcer, bile peritonitis, acute pancreatitis, urogenital diseases and uremia, and lead poisoning are worsened by the presence of paralytic ileus

Paralytic ileus may involve the entire intestine. Either the small intestine or the colon, however, may be separately affected Once distention has taken place, it may continue and increase Fluid and gas rapidly accumulate in the bowel Injury to the intestine occurs as a result of distention The distention causes edema, interference with venous return, and deprives the intestine of oxygen

SYMPTOMS The chief characteristic of paralytic or adynamic ileus is the abdominal distention, often of an extreme degree There is a dull continuous ache in the distended abdomen Nausea and vomiting are prominent The vomitus is of small volume but frequent in occurrence All fluids given by mouth are regurgitated. Bowel movements and the passage of flatus cease Enemas may be only slightly effectual With great distention there is limited respiration

EXAMINATION On examination the abdomen in paralytic ileus is distended, and no single loops of bowel can be felt The presence of definite abdominal tenderness and rigidity of the abdominal wall indicates peritonitis is present When paralytic ileus is not attended by peritonitis the tenderness is usually slight and not localized and the abdominal muscles are stretched by the distention but are not tense. The percussion note is tympanitic There is complete absence of any peristaltic sound The abdomen is not "silent" because almost always an occasional tinkle can be heard The tinkle is due to movement of fluid and gas in the distended loops of bowel, the movement being caused by respiration or other movements of the body. The "silence" of one of these abdomens is further broken by the presence of the breath and heart sounds which are well transmitted through the tense abdomen.

DIAGNOSIS The forementioned physical findings are diagnostic. Roentgenologic findings also have diagnostic value

Spastic Ileus Spastic ileus is a rare form of intestinal obstruction Any portion of the intestine may be involved There may be a small ringlike band of constriction

or there may be a spastic condition of a long segment of the bowel. The sex incidence is about equal

Spastic ileus occurs in psychoneurotic individuals. The symptoms consist of colicky abdominal pain, nausea, vomiting and constipation. The history is characterized by long periods of intestinal irregularity varying from constipation to diarrhea, flatulence and abdominal discomfort. Attacks of acute pain in the lower part of the abdomen associated with profound constipation alternating with watery diarrhea are common If the attack is prolonged, abdominal distention may occur as a result of dilatation of the intestine proximal to the contraction

Examination by physical means may in every way reveal all the signs of a mechanical obstruction of the intestine The difference in these abdomens from those affected by paralytic ileus is not in the abdomen but in the behavior of the patient. The psychoneurotic strives to convince all of the degree of his suffering. The patient with paralytic ileus is preoccupied with his sufferings and examinations are clearly extra burdens for him to bear.

The general condition of patients who have functional obstruction is good as compared with that of patients who have mechanical ileus which has been present for the same period of time This observation is often of diagnostic importance. In patients who have spastic ileus of the colon roentgenologic studies are necessary in order to rule out malignant disease

The task of differential diagnosis is lessened by obtaining a history of previous attacks which have subsided spontaneously Often these patients have had many operations, sometimes 30 or 40 of them

The patient usually recovers from the attack of spastic ileus After recovery everything except surgical exploration is done to establish the absence of organic intestinal disease In some instances death may occur from an attack.

Diseases of the Intestine Due to Disorders of Metabolism. ***Intestinal Carbohydrate Dyspepsia.*** Intestinal carbohydrate dyspepsia is said to be characterized by abnormal fermentation of carbohydrate in the intestine with excessive collection of gas during which there occur recurrent episodes of abdominal distention and pain and the passage of strongly acid, gassy stools. The incidence of this symptom complex cannot be appraised. Some physicians will not make such a diagnosis; others do

There are those who think that this syndrome is rather characteristic and believe that the excessive gas formation in the small intestine results from abnormal bacterial flora, for instance, an increase in gas-forming organisms and an extension of colonic flora into the small intestine or, to the contrary, a distal extension of the fermentation of carbohydrates into the intestine There is evidence which indicates a deficiency of diastatic enzymes which may be due to salivary, pancreatic, or succus entericus deficiencies

In intestinal hypermotility Owles demonstrated that there is almost invariably some failure in the total digestion of starch, whereas the digestion of fat and muscle fibers is less affected Hypermotility of the intestine may be induced by an excessive carbohydrate intake.

Further speculation in regard to the symptom complex of intolerance for carbohydrate is the postulation that there is interference with the capacity of the small bowel to absorb gases

The symptoms are characterized by intermittent attacks of borborygmi and explosive diarrhea lasting usually a few hours. The attack often is precipitated by eating rich candy, pancakes and honey, maple syrup or any other of a long list of rich carbohydrate or starchy foods However, the attacks may recur from time to time from even small amounts of starches and sugars.

The symptoms begin from 1 to 2 hours after the meal. There are audible peristaltic rushes, terminating in from 1 to 5 or 6 bowel move

hours after meals There may be abdominal pain if diarrhea is severe. Often there are anal burning and irritation after the bowel movement

Results of physical and roentgenologic examinations are negative The blood does not show constant or characteristic abnormality

The diagnosis is usually based on the history

Diseases of the Intestines Due to Unknown Causes. *Chronic Regional Enteritis.* Chronic regional enteritis is known also as terminal or distal ileitis, chronic segmental ileitis or enteritis, and ileitis with segmental colitis and ileocolitis.

Regional enteritis is a rare disease from which no one is exempt It is said that Hebrews are a little more likely to have ileitis than gentiles There is no good evidenc [illegible] and 40 years. Sex incidence is n[illegible]le It occurs in children and particularly in adolescents more frequently than it does in the aged.

The terminal portion of the ileum, for a distance varying between several centimeters and several feet, or at irregular segmental spacing throughout the entire small intestine, appears thickened and rigid The serosal surface may be obscured by an unusual extension of mesenteric fat and fibrinous exudate The serosa proximal to the most stenotic segment of the intestine on examination reveals engorgement of vessels and various degrees of hyperemia The maximal involvement is often in the terminal portion of the ileum just proximal to its junction with the cecum

In many instances the disease continues into the proximal portion of the colon or it may skip the terminal part of the ileum and the cecum to involve the ascending or transverse segments of the colon The disease in the colon does not differ pathologically from ordinary idiopathic ulcerative colitis

The mesentery of the involved ileum is thickened, boggy and edematous Fistulization in some cases has caused a matting of various intestinal loops to each other and to other structures in the neighborhood

On opening the affected intestine, it is observed that the wall of the bowel is thickened, the lumen narrowed, and mucosal ulceration, destruction and hyperplasia are apparent

Frequently the same characteristic pathologic lesions are found situated as far proximally as the jejunum.

SYMPTOMS The most annoying symptom to the patient is diarrhea Frequently intermittent in the beginning, it becomes more nearly constant as chronicity develops, but rarely is it severe, 4 to 6 bowel motions daily being an average number Crampy abdominal pain is as regularly recurrent a symptom as the diarrhea and in many patients more disabling

The pain is situated in the midabdomen or the lower right abdominal quadrant without definite time of onset or duration Pain, often crampy, often severe, may be the only symptom Inquiry will usually reveal that there have been loss of body weight, fever and diarrhea, perhaps of a mild degree at other times in the past

A loss of body weight and strength is a constant complaint A few patients who have regional ileitis will have fever and loss of body weight and strength without any other symptoms. An occasional patient who has regional enteritis or enterocolitis will manifest nutritional deficiency which will account for the major symptoms. A few who have regional ileitis will have no significant symptoms and though not in good health, will be suffering from no great inconveniences.

Symptoms of intestinal obstruction develop in many instances. In some the symptoms of obstruction appear in the absence of significant antecedent discomforts. It is often impossible in patients who seem to have had good health to make a preoperative diagnosis of the cause for the obstruction.

A suddenly occurring free perforation with peritonitis is rarely a part of the symptomatology in regional enteritis. Perforation of the bowel which progresses slowly with abscess formation is common and a prominent cause of symptoms in

regional enteritis. The abscess may remain localized and be eventually absorbed, but often an internal fistula forms which may communicate between adjacent segments of the bowel or finally reach the outside. In some instances, however, these events may occur or may have occurred with the production of but minimal symptoms. Often there has been slight loss of body weight, a mild fever with more frequent bowel movements, and general weakness and perhaps some increase in abdominal pain

The appearance of an external fistula, particularly after an operation for appendicitis in which drainage has been established, may constitute the major complaint in regional enteritis.

Perianal and rectovaginal fistulas are often present. The manner of development is not known If a fistula-in-ano is accompanied by chronic diarrhea, ileitis is suspected

Examination. There is evidence of loss of body weight and often there are dehydration and anemia. Abdominal tenderness which is increased in the lower quadrants of the abdomen is present. Often a mass is felt in the lower right quadrant of the abdomen In the mild form of the disease the abdominal examination will be essentially negative.

The tumor in terminal regional ileitis is irregularly nodular, firm, fixed, and so tender that margins cannot be delineated In some instances of the disease signs of intestinal obstruction will be present Physical signs of nutritional deficiency such as edema of hypoproteinemia and dermatitis indicate the chronicity of the disease

In many there will be present fever and an inflammatory mass in the lower right quadrant of the abdomen. The patient may be sufficiently ill at the time of the examination that time and special consideration may be necessary to exclude the presence of appendical abscess or right adnexal disease or perinephritic abscess.

If there should be perforation into the mesentery of the terminal ileum, a small abscess may form in the mesentery. In other instances, in which a fistulous communication has been established between the diseased segment and other abdominal structures, such as the sigmoid, cecum, another loop of small intestine, the uterus, vagina, or bladder, there may be an extensive or a very large mass or practically none at all on examination. Ordinarily these fistulas may be discovered by the roentgenologist, the surgeon or by the pathologist after the surgeon has finished.

In regional ileitis and ileocolitis a hypochromic anemia often is present. The mild anemia is usually not due to loss of blood In the average patient the leukocyte count is within normal range

[illegible] In instances [illegible] excluded and [illegible]

The prognosis seems to depend solely on the extent and the *intension of the* disease, irrespective of the treatment. The intension of the disease is determined by the severity of symptoms and rapidity of development of the complications In those who have amebic infections and ileitis, the ileitis is not materially improved by getting rid of the amebae In the absence of pulmonary tuberculosis intestinal tuberculosis usually can be excluded. Among children and adolescents an occasional one will be found in whom an extensive tuberculous enteritis or enterocolitis cannot be distinguished roentgenologically from ileitis

The longer the interval after operation, the greater is the incidence of recurrence.

Solitary Primary Ulcers of the Jejunum or the Ileum. Simple solitary or primary benign ulcers, which closely resemble peptic ulcers, occasionally occur in the jejunum or the ileum. The jejunal ulcers are the commoner of these rare ulcerations.

Jejunal Ulcer. Primary jejunal ulcer occurs in the proximal portion of the jejunum. In appearance the ulcer resembles peptic ulcer. The size of [illegible]ion varies

up to 2 cm. in diameter. More than one ulcer may be present. Heterotopic gastric or pancreatic tissue is not often found in the ulceration.

The patients may have as the manifestations those of spontaneous perforation Some of these patients, in giving the history, complain of postprandial pain relieved by the ingestion of food or alkalies More often the history reveals periodic abdominal distress at irregular intervals The pain is situated in the lower part of the epigastrium, around the umbilicus

On examination there is mild epigastric and midabdominal tenderness.

Roentgenologic studies of the small intestine, after the patient has ingested a barium meal, may establish the diagnosis of solitary ulcer in the jejunum These ulcers may perforate or form strictures. If these complications occur, their presence is diagnosed by the surgeon

Ileal Ulcer. Primary ulcers of the ileum, as recorded by Brown, occur in the lower 3 feet (0 9 meter) of the ileum. Heterotopic tissue is not found in these ulcers These lesions may perforate, or bleed Bleeding and anemia were the outstanding features in more than one half of Brown's cases.

Nausea and vomiting, and pain situated in the lower part of the epigastrium, around the umbilicus, or in the lower right abdominal quadrant, are common. The pain, of a colicky type, is often referred to the back, and is not relieved by antacids. The ingestion of food may aggravate or relieve the pain or may have no effect on it. Apparently the foregoing symptoms are not severe, for the majority of patients seek relief for perforation and peritonitis, obstruction, melena, and anemia.

Results of the examination are often negative In some of these patients the spleen is palpable, and in some, aside from the enlarged spleen, distinctive physical findings are lacking.

Roentgenologic examination may be diagnostic. In others the ulcer is found on exploration for Meckel's diverticulum which is not present.

Tumors of the Small Intestine. Many of the lesions of the small intestine, such as small benign tumors, are discovered at necropsy as incidental findings which have not given symptoms

Benign Tumors of the Small Intestine. Benign tumors of the small intestine occur most frequently in the duodenum and the ileum In the order of the frequency of their occurrence the following benign tumors are listed. (1) adenomas and pancreatic rests which enlarge, these occur with equal frequency and together constitute by far the greatest number of the benign tumors; (2) myomas, adenomyomas, fibromyomas and osteochondromas, (3) lipomas, (4) angiomas and hemangiomas; (5) cysts and cystadenomas, all of which are of rare occurrence even in the over-all number of benign tumors

The *symptoms* of manifested tumors of the small intestine are rapid loss of weight, anemia and bleeding, or symptoms due to intermittent or total intestinal obstruction or intussusception

In the usual instance of a tumor of the small intestine the obstructive symptoms are of insidious onset In the beginning there is a mild colicky abdominal pain perhaps associated with slight distention and often with nausea and, at times, vomiting The insidious progressive type of intestinal obstruction is seen in cases of sarcoma, carcinoma, carcinoid tumor, lipoma, hemangioma and cysts. Tumors growing extraluminally may not give rise to obstruction until they have attained considerable size These large tumors cause a failure of the general health, often before a palpable mass is present and before obstruction occurs

Ulceration of a benign tumor may cause attacks of pain due to spasm and irritability of the intestine. In some instances the first complaint depends on the development of an abscess or a fistulous communication between the lumen of the intestine and the necrotic center of an extraluminal growth. A free perforation due to ulceration or necrosis is a rare first indication of tumor of the small intestine.

The general physical examination is negative in the absence of complications of benign tumors of the small intestine. When complications are present these may often be revealed by the findings on general examination.

Diagnosis is established by roentgenologic examination In some instances the diagnosis is not made until surgical exploration is done in order to determine the cause of the abdominal symptoms.

Malignant Tumors of the Small Intestine. *Carcinoma.* Malignant tumors of the small intestine are uncommon The average age of patients who have carcinoma of the small intestine is about 10 years less than the average age for patients who have gastric cancer. These tumors may occur before the age of 40 years. Two men are affected to each woman who has a carcinoma of the small intestine.

In the recorded experience of Pridgen, Mayo and Dockerty the adenocarcinoma occurs most frequently in the jejunum and decreases in the middle section of the small intestine with another increase in incidence in the ileum. The lesions are annular, ulcerative and polypoid in types. The annular type is the commonest. Proximal to the lesion the bowel often is dilated In extreme dilatation of the bowel perforation may ensue In instances of polypoid lesions intussusception may be present. Metastasis to the liver and cervical lymph nodes may be present

This rare disease is commoner in men than in women The greatest incidence of the disease is between 45 and 50 years of age Bleeding is the most important symptom of cancer of the mesenteric small intestine It may be manifested as occult blood in the stools, as an unaccountable hypochromic anemia, or as a massive hemorrhage producing large, tarry stools. Mechanical obstruction is responsible for the subjective complaints of many patients who have intestinal carcinoma. The symptoms in some patients who have intestinal obstruction are gradually progressive, beginning with intestinal colicky pain and slight nausea, followed by increasing abdominal distention, visible peristalsis, nausea, vomiting and constipation. The onset of symptoms in other patients who have intestinal obstruction may be abrupt when there is a rapidly developing mechanical obstruction Intussusception of a pedunculated carcinoma and, less frequently, the torsion or knuckling of a loop of bowel may be responsible for the acute obstruction. The onset in still other patients may be that of a localized peritonitis or a subacute perforating peptic ulcer

When the symptoms of carcinoma of the jejunum and of the ileum have become manifest, the roentgenologic demonstration of the lesion is usually easy.

Carcinoid Tumors Carcinoid tumors affect persons in the older age groups and may be responsible for disabling symptoms. They also may affect middle-aged persons

Carcinoid tumors tend to involve the terminal segments of the ileum as small, submucosal nodules with minimal ulceration. In half of 30 cases reported by Dockerty and Ashburn in which accurate information was available, the tumors were multicentric Infiltration was a pronounced feature as regards submucosa, muscularis, peritoneum, nerves, lymphatic spaces and blood vessels. Puckering and kinking in the region of tumor invasion provided a possible valuable roentgenologic sign of identification Involvement of regional nodes was observed in 11 cases and hepatic metastasis in 5 instances Evidence was afforded on the basis of microscopic studies that all carcinoid tumors are in essence peculiar, low-grade (grade 1, Broders) adenocarcinomas. In 13 of these 30 cases there was undoubted evidence of metastasis.

The symptoms may be indistinguishable from those of a carcinoma. The symptoms may be those of intestinal obstruction caused by a knuckle-shaped kink formed by a carcinoid in the bowel.

The roentgenologist may have suspected the correct diagnosis He usually reports an obstructing lesion. However, the diagnosis cannot be made except by histologic study of the tissue.

Sarcoma. Sarcomas are variously classified by the pathologists [illegible] leiomyo-

sarcoma, (2) fibrosarcoma, (3) angiosarcoma, (4) malignant lymphoma and (5) malignant melanoma.

In most respects sarcomas (leiomyosarcoma, fibrosarcoma and angiosarcoma) and carcinomas are similar from the standpoint of their clinical manifestations.

The malignant lymphomas among the sarcomas tend to occur oftener in younger persons than do carcinomas; this is true more of the localized forms which involve the colon than of the forms involving the rectum The clinical course of sarcoma in most cases is rapid, and the duration of symptoms from the onset until the patient is hospitalized is, on the average, shorter than for carcinoma.

Abdominal pain tends to occur earlier in sarcoma and perhaps is more severe than it is in carcinoma Bleeding is less frequent than it is in carcinoma. Obstructive features are also less prominent because of the tendency of sarcoma to dilate the lumen of the bowel.

On examination often there are present fever, emaciation, pallor and debility which have developed more rapidly in association with sarcoma than they do with carcinoma Masses are palpable more often and usually are larger and more extensive in patients who have sarcoma than in those who have carcinoma. In contrast to the condition when carcinoma is present, digital examination of the rectum in patients who have sarcoma often reveals an intact mucosa over the tumor.

Lymphoblastomas of the stomach and intestines are described in association with diseases of the hemic system (Chapter 12)

Melanoma. Melanoma is rarely if ever primary in the small intestine. Melanoma of the intestinal tract is ordinarily secondary to a cutaneous pigmented lesion or a melanoma of the retina or rectum Secondary growths may appear in the intestinal tract without evidence of metastasis elsewhere.

In a patient who has malignant melanoma, pigmentation of the anal orifice may be seen, resembling the appearance of external thrombotic hemorrhoids Very suggestive of a pigmented lesion is a blackish discharge which may be obtained on the examining finger.

In some cases of intestinal melanoma, years have elapsed between the removal of an external growth and the appearance of the intestinal tumor The possibility of intestinal melanoma is considered only if symptoms of intestinal obstruction or bleeding occur in a patient who has previously had a pigmented tumor removed from elsewhere in the body

Diagnosis of Tumors of the Small Intestine. In the diagnosis of tumors of the small intestine, malignant, as well as benign, tumors in the duodenum capable of causing symptoms are demonstrated by roentgenologic examination In the rest of the small intestine greater difficulties are encountered by the roentgenologist. If persistent bleeding or symptoms suggestive of partial obstruction are present, roentgenologic studies, if negative, should be repeated If the roentgenologic findings are consistently negative, the diagnosis may have to be postponed for the surgeon to make when he explores for the cause of the illness If intestinal obstruction is present or impending it is unsafe to put barium into the small intestine

THE VERMIFORM APPENDIX

Development of the Processus Vermiformis and the Ileocecal Valve (Incompetent Ileocecal Valve) The ascending colon begins slowly to elongate at about the middle of fetal life The cecal bulge grows, extending as a blind sac beyond its junction with the terminal ileum The extension of the cecum beyond this junction is at first a pointed, horn-shaped projection The distal end of this transitive projection extends rapidly f[illegible]
at this p[illegible]
its point[illegible]
pointing in that direction When the appendix is at the top of the cecum, these variations

in the size and shape of the cecum are differentiated by the roentgenologist from contractions of the cecum as the result of an inflammatory process.

Normally, during the lengthening process of the cecum, the cecal walls become thinned There is a diverticularization of the thinned walls, which flex and rotate medially and downward. These movements of flexion and rotation form the ileocecal valve. Whether or not the ileocecal valve is competent in adult life depends on completion of the processes of (1) dilatation, (2) flexion and (3) rotation. There cannot be a competent ileocecal valve in the presence of a fetal type of cecum

The appendix may be absent. It may be excessively long or short. It may be situated in any part of the abdomen in association with varying degrees of failure of rotation of the intestines In situs inversus viscerum it is on the left side of the abdomen

POSITION OF THE APPENDIX (PROCESSUS VERMIFORMIS). The position and direction of the normal appendix have been variously described and much discussed, owing to the fact that the appendix is so curled, curved, and twisted on itself that it is impossible to say that it points in any definite direction, and that, being so mobile, it may be found in almost any position, swinging around with its point of attachment to the cecum as the axis This point being its axis, the greatest displacements of the appendix in the abdomen depend on the situation of the cecum.

Diseases of the Appendix Due to Prenatal Influences. Congenital malformations of the appendix are rare and consist of complete absence, a double appendix, and so-called split appendix

Diverticula of the appendix may be single, but usually they are multiple. The commonest location is along the mesenteric border or in the distal half of the appendix Importance is attached to them for their presence in association with acute appendicitis since the thin wall of the diverticulum is less able to withstand infection and increased tension without rupture than is the normal appendical wall Their presence in association with pseudomyxoma peritonaei is not understood

Polyposis of the appendix may occur, but because of its rarity little is known concerning this condition In congenital disseminated polyposis of the colon the appendix is often free from polyps.

Appendicitis. Appendicitis is a bacterial infection which often seems to have been predisposed by local mechanical factors Heredity, diet, race, season, pregnancy, trauma and foreign bodies are unimportant etiologically. The sexes are affected equally. The disease occurs most commonly in adolescence and early adulthood but no person, regardless of age, may be exempt from an attack of appendicitis.

Irritation secondary to the presence of *Oxyuris vermicularis* or other intestinal parasites often has been recorded as a cause of appendicitis Like foreign bodies, parasites in the appendix may be of little significance A worm may simply like to live in the appendix

Acute appendicitis may occur during the course of acute viral or bacterial contagious diseases for instance, measles, mumps, varicella and scarlet fever. Appendical involvement may occur in association with rheumatic fever and periarteritis nodosa, not as a true acute appendicitis but as a rheumatic involvement or as a periarteritis of the vessels of the appendix. During the course of many an acute infection, for instance, pneumonia, symptoms of appendicitis may appear The signs and the symptoms of appendicitis may occur during the course of acute porphyria and during acute hemolytic crises, particularly in sickle cell anemia.

There are two sources of infection available to the appendix, (1) the enterogenous and (2) the hematogenous Acute appendicitis, in by far the greater number of cases, is of enterogenous origin Appendicitis due to hematogenous infections may occur during septicemia, go unobserved, and be found at postmortem examination.

It is now recognized that often the cause of abdominal symptoms identical with

those of appendicitis may be mesenteric adenitis from any cause However, it is well to know that mesenteric adenitis may accompany acute appendicitis.

PATHOLO [illegible]
(1) acute c [illegible]
abscess, (4) [illegible]

SYMPTO [illegible]
vomiting A [illegible]
midabdominal pain. Nausea and vomiting tend to subside as the pain becomes localized over the appendix The pain and its intensity constitute the most important symptom of acute appendicitis

Constipation is the commoner state of the bowels in adolescents and in adults. Diarrhea is commoner in young children

The temperature is rarely more than 100 F (37 8 C). It has been thought that the more severe the disease of the appendix, the higher will be the febrile reaction. The height of the fever is not a trustworthy guide to the severity of appendicitis. In the event of perforation of the appendix and local abscess formation, however, the temperature often reaches 101 F (38 3 C) The fever tends to be higher in children than in adults. In the aged, appendicitis may be present without fever.

Increase in the pulse rate has some relation to the rise in temperature. The pulse rate rarely exceeds 100 beats per minute unless gangrene or perforation of the appendix has occurred. In adults, when the pulse rate exceeds 110, perforation of the appendix should be suspected and is usually found to be present.

The cessation of localized abdominal pain which previously had been severe usually signifies a termination of the acute process, gangrene or perforation is likely to be present when the pain subsides quickly, especially if the pulse rate does not decrease and the temperature does not subside.

EXAMINATION. There is tenderness in the right lower abdominal quadrant at McBurney's point, which is situated approximately just below the junction of the middle and outer thirds of a line drawn between the anterior spine of the iliac crest and the umbilicus The region of maximal tenderness varies according to the situation of the appendix in the abdomen In failures of intestinal rotation and fixation of the intestines, the point of tenderness may be situated almost anywhere in the abdomen. When the appendix is low in the right side of the abdomen, the pain may be lower in the abdomen, or in the right flank or the back In a pelvic appendix the point can best be palpated on rectal or vaginal examination When peritoneal irritation is widespread the tenderness becomes more diffuse, and accurate localization is not possible. Innate rigidity of the abdominal muscles, which often is present in ticklish and in neurotic individuals, or the lack of co-operation of the patient adds an uncontrollable hazard to localization of tenderness

Various physical signs which are often manifested in some of those who have appendicitis have been described as indicating degrees of infection or differential diagnostic points These signs are of no great diagnostic value and they would be detected and correctly interpreted even if their names were unknown

1 Irritation of the parietal peritoneum by the inflamed appendix permits *rebound tenderness* to be elicited To test for rebound tenderness a steady, firm pressure is applied over the region of tenderness When the pressure has been firmly applied, the examiner's hand is suddenly removed The patient then evinces the sharp pain thus induced When muscle guarding is present, rebound tenderness cannot be elicited This test is seldom necessary It is punishment to those who have appendicitis

2 Rigidity of the abdominal wall, or *muscle guarding,* may be detected by applying firm pressure with the palm of the hand When present and not due to nervous factors, it is a sign of peritoneal irritation It is usually limited to the quadrant or region in which the disease is situated

3 Hyperesthesia of the skin overlying an acutely diseased appendix or any other acutely inflamed viscus is usually present This finding is of value in diagnosis if sufficient

time is spent to be sure of the presence of the hyperesthesia and the examiner is well enough experienced to interpret the vagaries of overlapping cutaneous nerve innervations.

4 *The prone test for diagnosis of retrocecal appendicitis* consists in palpating the abdomen with the patient lying face downward. If acute retrocecal appendicitis is present, gentle palpation of the right lower quadrant of the abdomen with the patient prone will elicit greatly increased tenderness, serving to differentiate the appendicitis from pelvic and renal lesions Too much dependence should not be placed on this test because the results are often positive in colitis and ileitis.

When the appendix is retrocecal, as it often is, the pain may be more intense in the right flank or right renal region

Always included in descriptions of the physical findings in acute appendicitis, but of rare occurrence, are (1) an acutely inflamed appendix producing irritation of the psoas muscle and giving rise to pain on the anterior and inner aspects of the right thigh; (2) an acutely inflamed appendix resting on the ureter and giving extension of pain into the bladder or scrotum, dysuria and desire for frequent micturition, (3) an inflamed appendix situated low in the pelvis, causing pain lower down in the abdomen and in the left lower part of the abdomen, and (4) an inflamed appendix in contact with the sigmoid or the rectum and sometimes producing desire to defecate, painful defecation, or pain extending to the back of the pelvis or to the perineum.

Always too it is emphasized to elicit the knee reflexes lest a tabetic crisis be called appendicitis and operation be advised

On rectal examination of one half of the patients who have acute appendicitis, tenderness may be elicited high in the right side of the pelvis. The rectal examination is particularly valuable in children, in whom the relatively shallow pelvis permits a much higher level to be reached than is possible in the rectal examination of adults Bilateral tenderness from acute appendicitis is rare, and when present it often indicates a pelvic abscess or pelvic peritonitis from appendicitis or salpingitis.

Urinalysis is a routine procedure before any definite conclusions are made in regard to the presence or absence of appendicitis The results are usually negative in appendicitis An occasional erythrocyte in the urine is not significant Definite hematuria indicates urogenital disease, usually a calculus of the kidney, ureter, or bladder It is true that on rare occasions an inflamed appendix involves the ureter, but this is so exceedingly uncommon that a hematuria must be considered to arise from urogenital disease, hypothetic assumptions should not be made to justify the diagnosis of appendicitis Pyuria likewise is infrequent in acute appendicitis, but if the patient is a female, an aged man or a child and pyuria is present, a catheterized specimen should be examined to exclude contamination of the urine If the urine appears pink or if the patient appears to be jaundiced a hemolytic crisis is suspected.

A normal total leukocyte count may be present even in patients who have severe appendicitis The leukocyte count is a most valuable laboratory procedure when used repeatedly while a patient is under observation for appendicitis If the trend of a series of leukocyte counts is upward, this trend is significant of an advancing infection and thus may be helpful in making a diagnosis In children the leukocyte count averages 2,000 cells per cubic millimeter of blood higher than in adults during the same phase of the disease Usually there is a high percentage of neutrophils present. When the number of leukocytes exceeds 20,000 per cubic millimeter of blood, unless peritonitis is present serious consideration should be given to diseases other than appendicitis, particularly to lobar pneumonia in the basilar lobe of the right lung.

Diagnosis of Acute Appendicitis. Epigastric or midabdominal pain, preceded or followed by nausea and vomiting, with the pain tending to localize after an hour or so in the right lower quadrant, generally is appendicitis if the appendix has not been removed, or if the patient is not a colored man with sickle cell anemia, and it is good judgment to consider it so. Anorexia is always associated with the pain. When the pain localizes in the lower right abdominal quadrant, it tends to

become constant. The intensity of the symptoms increases until the appendix ruptures or until the attack spontaneously subsides

The differential diagnosis of acute appendicitis may require a consideration of all the acute conditions which occur in the abdomen In women of the childbearing age, diseases of the genital organs are of immediate differential diagnostic importance. These diseases may be enumerated acute salpingitis, rupture of a graafian follicle (mittelschmerz), torsion of an ovarian cyst, a pedunculated fibroid of the uterus, a cyst of the hydatid of Morgagni, an ovary with a long mesenteric attachment or a ruptured ectopic pregnancy Likewise diseases of the urinary organs, namely, ureteral calculus, pyelitis of the right kidney, and intermittent hydronephrosis of the right kidney are to be considered Finally the blood dyscrasias prone to be complicated by hemolytic crises, especially sickle cell anemia, must be considered

The prognosis in cases of acute appendicitis is largely dependent on the complications

Immediate surgical operation is indicated for an acute appendical inflammation which seems to be progressing An interval of delay in operating is indicated for a subsiding acute or recurring subacute appendicitis, and for the localized abscess.

The mortality rates given by different statistical studies range so widely that they are hardly worthy of recording The surgical mortality rate in uncomplicated appendicitis is from 1 to 2 per cent

Acute Appendicitis in the Aged An elderly patient who has an acute appendicitis may not appear seriously ill even during the early stage of peritonitis There are digestive symptoms attributed to dietary indiscretions. Anorexia, nausea and vomiting may be present Abdominal pain is not severe and tends not to localize Often there is little or no fever Many of these patients are not seen until peritonitis has developed Gangrene, perforation and peritonitis develop rapidly Due to the advanced stage of the appendicitis when the patient is first examined it can easily be confused with intestinal obstruction, and time may be lost in attempts to locate a growth.

On physical examination slight or moderate distention of the abdomen with little or no tenderness will be observed Commonly laboratory data are unreliable either for diagnosis or as a measure of the severity of the disease

The diagnosis cannot be made unless there is some localization of pain and tenderness over the appendical region accompanied by a moderate leukocytosis.

Acute Appendicitis in Children In a child an acute infection of the upper part of the respiratory tract often precedes appendicitis In contrast to the symptoms *in adults, diarrhea may be present*

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be a [illegible]

left alone. Even in the presence of generalized peritonitis the abdomen, although distended, may be soft and tenderness may be slight.

The diagnosis of appendicitis in children is more dependent on the rectal examination than in adults, since in children a much greater part of the abdomen is within reach of the palpating finger The laboratory findings of blood counts and, in some cases, of a bacteriologic study of the peritoneal fluid are valuable diagnostic assets

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acute appendicitis in children are acute hip disease, osteomyelitis of the femur and ilium, psoas abscess, inguinal or femoral lymphadenitis, gastroenteritis, intussusception, and inflammation of Meckel's diverticulum

COMPLICATIONS OF ACUTE APPENDICITIS. The signs of abscess in the early stages of its formation are not definite because there is present no localization of findings, and it must be decided whether the appendix is ruptured or not. If the process is localizing, a rectal examination will sometimes enable the examiner to palpate this localizing process A decrease in the temperature and a lessening in the degree of leukocytosis may indicate localization. Usually fully formed appendical abscesses cannot be diagnosed if they are not in the usual places. The unusual situations for appendical abscesses are retrocecal or subhepatic. In these situations a preoperative diagnosis is impossible.

Hepatic abscesses, although *rare, are serious complications of appendical abscesses* One third of all perihepatic and subphrenic abscesses are caused by a ruptured appendix

Formation of fistula and sinus may eventually occur when an abscess forms. *Inclusion in the wall* of an appendical abscess of part of a hollow viscus, such as the cecum, urinary bladder, sigmoid, or rectum, may result in rupture of the abscess into that organ with fistulization

When acute appendicitis is complicated by adhesions, formation of abscess, or peritonitis, intestinal obstruction and paralytic ileus are common.

Extension of infection from the appendix may result in thrombophlebitis of the iliac or femoral veins, from which may be released an embolus which lodges in the lungs. If the embolus is large, death quickly ensues. Emboli may form in these veins during the course of appendicitis without detectable extensions of the infection.

CHRONIC APPENDICITIS. RECURRING APPENDICITIS. There is no agreement as to what should be considered chronic appendicitis Such a condition no doubt exists, but it cannot be diagnosed. Recurring appendicitis is simply repeated attacks of acute appendicitis

Mucocele of the Appendix. Mucocele of the appendix has been known also as colloid or pseudomucinous cyst, hydrops mucinous cyst, myxocele and pseudomyxoma of the appendix. Mucoceles vary in shape and size. Their contents consist of a mucoid material which may be thick or thin but ordinarily is viscous, stringy and tenacious.

A mucocele of the appendix forms when there is obstruction of the lumen of the *appendix, and the contents of the lumen remain sterile.* The continued secretion of the mucosa of an appendical stump, inverted at the time of surgical removal of the appendix, is a common cause of the formation of mucocele.

Most mucoceles are discovered and removed during an operation performed because of some other disease. The roentgenologist often diagnoses mucocele. Only rarely do mucoceles become large enough to be palpated through the abdominal wall, and then the diagnosis of tumor in the right lower abdominal quadrant is usually made Surgical removal is the only treatment.

Carcinoid (Argentaffine) Tumors of the Appendix. The cytoplasmic granules of the chromaffin cells of the intestine are capable of reducing silver compounds to brown-black particles, and this reaction accounts for the name argentaffine tumors, for these tumors arise from argentaffine cells. These cells are more numerous *in the appendix and the terminal portion of the ileum* than in any other part of the intestine.

Carcinoid tumors of the appendix occur in both sexes, in patients of various ages from childhood to senility, inclusive They are found most frequently in adults less than 35 years of age.

Carcinoids are found in all situations, ranging from the cardio-esophageal junction to the rect[illegible] result of chronic inflammatory processes. [illegible] m, where the incidence of origin [illegible]

Regardless of size, point of origin, or presence or absence of metastasis, carcinoids

possess essentially the same microscopic features of cytologic differentiation and histologic architecture. Origin from, and differentiation into, glandlike structures is a constant observation. All these tumors are of grade 1 malignancy (Broders).

Appendical argentaffine tumors usually are discovered at the time of appendectomy. Rarely do these tumors metastasize. Carcinoid tumors of the ileum involve only a part of the lumen. They cause intestinal obstruction and they may metastasize to local lymph nodes.

The prognosis following complete removal of these growths is usually good. However, these tumors are not benign

THE COLON

The colon performs no important digestive functions. The colon absorbs water and electrolytes from the intestinal chyme passed along to it from the ileum. When the body is deprived of the colon the kidneys immediately assume this function. The other function of the colon is one of convenience storage of the dejecta to be evacuated at some convenient time which is dictated by custom and habit

The large intestine comprises (1) the cecum and appendix, (2) ascending colon, (3) transverse colon, (4) descending colon, (5) sigmoid flexure, composed of the iliac colon and pelvic colon and (6) the rectum and anal canal

The length of the large intestine exclusive of the rectum and anal canal is 4 feet 6 inches (137 cm) in the female, and 4 feet 8 inches (142 cm) in the male

The position of the colon cannot be accurately predicted

Size of the bowel is an undependable criterion in distinguishing the large intestine. There are three longitudinal bands (taeniae coli) on the colon, from 1/4 to 1/2 inch (6 to 13 mm) wide, according to the amount of distention.

The sacculations of the colon are produced by the longitudinal bands being one-sixth shorter than the rest of the tube Although sacculation tends to become less marked on distention, it is still a valuable means of identification. Dividing the longitudinal bands will cause the sacculation to disappear and the gut to lengthen Diverticula of the colon are common after the age of 40 years

Appendices epiploicae, or the small tags of peritoneum containing fat, are found along the large intestine as far as the rectum They are most numerous along the inner longitudinal band and the transverse colon These are often the site of diverticula and thus diverticulitis or appendicitis epiploicae.

Often the cecum and the descending and sigmoid colons are normally palpable. The colon cannot be outlined by percussion

Diseases of the Colon Due to Prenatal Influences. *Primary Megacolon.* This disease is known also as Hirschsprung's disease, idiopathic dilatation of the colon, and congenital dilatation of the colon

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The name Hirschsprung's disease has been used to designate extreme dilatation of the colon of congenital origin occurring in infants and young children, primary megacolon with the same clinical and morphologic features is seen in adults. It is not known whether or not all instances of the condition among adult persons are due to a primary congenital defect

Swenson and his associates have contended that the primary lesion in megacolon is in the distal, nondilated segment Despite this contention, grossly this portion of the colon or rectum appears normal They demonstrated to their satisfaction that, in control patients, groups of strong peristaltic waves progress from the transverse colon to the anus. The authors have expressed the belief that the absence of normal propulsive waves in the rectum and rectosigmoid constitutes a physiologic defect that results in chronic obstruction

Among the neurogenic causes there is an absence of parasympathetic ganglion cells in the distal strictured segment of the colon

Grossly, the involved segment of bowel is dilated and elongated and its walls are thickened The sigmoid colon is the segment commonly affected. In some of the more advanced instances the whole colon is involved, the dilatation of the intestine ending abruptly at the ileocecal junction. Usually the mesentery of the sigmoid is greatly elongated and thickened Chronic inflammatory changes are frequent and may be manifested by hyperplasia, necrosis of the surface membrane from fecal pressure, and actual stercoral ulcerations

Primary or idiopathic megacolon has been reported in persons of all ages from birth to 80 years. Familial incidences have been observed. Boys and men are more *commonly affected than girls and women*

SYMPTOMS Megacolon may not produce severe symptoms in the older child or adult and may be discovered accidentally by roentgenologic examination of the colon made because of some other condition. The two constant symptoms are obstinate constipation and enlargement of the abdomen.

The constipation, dating from birth, may be the chief and only complaint Many days, weeks, or even months may elapse without a bowel movement, and without local or systemic symptoms attributable to the long period of intestinal inactivity. In instances of milder megacolon, bowel movements occur at irregular intervals, causing no inconvenience The stools, when they do occur, vary greatly in consistency and in size and shape Large globular masses are often passed. Cathartics and enemas have little effect Intermittent intestinal obstruction is present from time to time There may be frequent small rectal discharges unassociated with symptomatic relief and accompanied often by tenesmus and frequent desire to defecate

Abdominal pain is rarely severe in the absence of a complication such as volvulus or peritonitis The chronic character of the distention probably accounts for the relative lack of subjective complaints.

In instances of severe long-standing megacolon, symptoms indicative of loss of weight, asthenia, and prostration occur. Fever is not present unless there is secondary infection, pneumonia, volvulus, or complete intestinal obstruction

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spaces are widened and the subcostal angle is obtuse. The lateral walls of the thorax bulge. Distention of the skin causes atrophic changes. The skin is shiny, glazed and dry The superficial veins are visible Edema of the feet and legs which often is present may be caused by the pressure of feces and gas in the colon.

Peristaltic movement may be seen Fecal masses may be palpated in the abdomen or during the bimanual examination of the rectum, or they may be detected only by ballottement during the examination.

On percussion the abdomen is uniformly tympanitic Hepatic dullness is absent or diminished. The tympany extends to, and often includes, the lower part of the left side of the thorax, anteriorly, laterally and posteriorly There is no evidence of shifting dullness, because ascites does not accompany megacolon

In some children and often in adults there are no signs on physical examination and the condition is found during the routine sigmoidoscopic examination in search for the cause of the constipation.

DIAGNOSIS. A diagnosis of megacolon is established by sigmoidoscopic examination or by roentgenography after a barium enema A differentiation of congenital ... of the anal

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In the absence of complications the prognosis for patients ... 4 or 5 years of life is fairly good Megacolon occurring in older children and in adults seems to have little effect on life expectancy. In most patients a colonic regimen can be employed which permits of health. If health cannot be maintained

on such a program, resection of the involved segment of the colon or of the entire colon should be recommended.

Acute Infections of the Colon. ***Shigella and Shigellosis (Bacillary Dysentery).*** Organisms of the genus *Shigella*, family Enterobacteriaceae, are the etiologic agents of bacillary dysentery. Some species occupy doubtful positions, while still others are nonpathogenic for man

All species of *Shigella* tend to be antigenically heterogeneous Serologic overlapping between species is common. Antigens present in certain species of *Shigella* have been detected in other enteric bacilli. Despite these irregularities in antigenic structure, classification of *Shigella* depends on serological results

The *Shigella dysenteriae* and *Shigella ambigua* are antigenically homogeneous These organisms cause a severe dysentery. The para-Shiga group comprises three main subdivisions, namely, (1) Flexner's bacillus, (2) Hiss and Russell's "Y" bacillus and (3) Strong's bacillus These are antigenically heterogeneous, and at least five types have been recognized. These types are referred to as paradysenteriae V, W, X, Y and Z. The *Shigella sonnei* is heterogeneous and two antigenic types are recognized. These organisms are nonpathogenic. Four types of *Shigella dispar* have been distinguished The antigenic structure of *Shigella alkalescens* is complex These organisms contain at least five antigenic components A, B, C, D and E A is species specific, B, D and E are coliform and paracoliform bacilli, while C is found in *Shigella paradysenteriae* as well as in *Shigella alkalescens*. These organisms are nonpathogenic in man

The National Institutes of Health has maintained a field laboratory for the investigation of the acute diarrheal diseases A total of 8,643 survey fecal cultures was obtained on representative persons Institutional inmates, among whom clinical disease and subclinical infection were relatively common, have been studied, using new, highly selective culture mediums which increase the reliability of bacteriologic findings

The proportion of adult patients who have endemic diarrheal disease whose stools were found culturally positive for *Shigella* by The National Institutes of Health was 76 per cent of those who had severe disease and 58 per cent of those who had milder disease There was an increase in the proportion of those with positive fecal cultures as the number of examinations during illness increased The percentage with positive findings was lowest for the group whose ages were less than 6 months, but the percentage varied widely with area and with severity of illness. The cultural findings for institutional inmates were similar

This study by The National Institutes of Health seems to indicate that the cause of diarrheal disease varies with area, with season and with age of persons concerned.

The *Shigella paradysenteriae* infections vary in incidence and occur more frequently than is usually thought, especially in the younger age groups These infections seem to be more frequent in infants less than 2 years old than in older patients. The rate declines thereafter, with fewer instances among adolescents and adults.

Among the general population the cases occur chiefly during the summer and early autumn There is a pronounced concentration of incidence among the poor

convalescents are carriers The average duration of the convalescent carrier state in 50 per cent of the cases is one month In some instances the carrier states may last a year Chronic carriers, if there are any, are exceedingly rare The passive carrier state is unusual at ages of less than 1 year but increases in frequency with age More than one half of the children infected at 3 years and most of the infected older children and adults are passive carriers It is therefore not surprising that diarrheal diseases commonly appear sporadically The mode of spread is mainly by a direct or an indirect person-to-person distribution of the infecting organisms.

Often there is no evidence which suggests that the etiologic agents responsible

for the diarrheal disease are brought into the household in water, milk or any other food product. The disease and flies are often found in the same environment, but there is no good evidence that flies are important in the dissemination of *Shigella*.

PATHOLOGY. The pathologic changes of bacillary dysentery are limited to the colon and the terminal ileum The first changes are observed through the sigmoidoscope and consist of transverse red swollen ridges. The mucosa is red and presents small diffuse scattered hemorrhagic areas interspersed with purpuric spots beneath the mucosa The inflammation involves the mucosal glands, the mucosa swells and thus a granular appearance is imparted. In the acute severe instances of the disease the entire mucous surface may become necrotic and a membrane forms. During healing or after the acute process has healed, retention cysts in the mucosa may be formed and may remain for several weeks or a month or more. From the fluid of these retention cysts may be cultured the dysentery organisms These cysts are the means of the production of carriers

During the acute stages there is cloudy swelling of the liver, kidneys, and heart as the result of the fever The mesenteric lymph nodes of the colon are swollen and soft Splenic enlargement may be present and there may be focal necrosis Organisms of the genus *Shigella* rarely if ever produce a septicemia. They remain limited to the colon and the lower segment of the small intestine.

SYMPTOMS The incubation period of bacillary dysentery may be as short as a half a day or as long as 7 days, the average being 2 days. The acute phase of the disease is self-limited to about 12 to 14 days.

There are variations in the number of bowel movements from a few loose stools daily to continuous tenesmus and involuntary passage of liquid feces. The most common and clinically the most important form of the disease is that manifested by a mild diarrhea The onset may be so insidious that it is difficult to determine accurately when the illness began

In the moderately severe forms of the disease the onset is often abrupt with colicky abdominal pains and diarrhea with or without fever. The abdominal pains and tenesmus steadily increase. The dejecta from the bowels contain mucus and blood. The discharge of blood and mucus often is not excessive and grossly may not be detectable Dysuria may be severe and, if so, diagnostically confusing Likewise severe abdominal pain may arouse suspicion that appendicitis or gallbladder disease is present.

Bacillary dysentery may commence with severe colicky abdominal pain and vomiting which are followed shortly by diarrhea and tenesmus Stools vary in number from 10 to 60 per day. The stools at first contain some fecal material, but within 24 hours they will consist of clear, tenacious, viscid mucus streaked with blood. Fever may vary widely, being remittent or constant. It sometimes rises to 104 F (40 C). In some of the seriously ill patients the prostration is so severe that no rise in temperature occurs. In the critically ill the temperature is subnormal. The dehydration, continued desire to defecate, and straining of tenesmus completely exhaust the patient. These symptoms tend to subside when hydration is accomplished by parenteral administration of fluids

Relapsing forms occur. Exacerbations return with great regularity but with symptoms less severe than the original ones. The effects on body nutrition of several relapses may be disastrous

EXAMINATION. The findings on physical examination depend on whether the disease is mild without physical findings or severe with dehydration, mental confusion, increased pulse rate and low blood pressure Generalized abdominal tenderness and definite muscle guarding are present in severe bacillary dysentery.

In the acute stage of bacillary dysentery, roentgenologic examination is impos- ... medium.

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findings that can be distinguished from those present in chronic nonspecific ulcerative colitis

The sigmoidoscopic findings are not definitely diagnostic of the type of dysentery present. In all types of bacillary dysentery there are red, swollen transverse ridges. The mucosa is reddened and there are present diffuse scattered hemorrhagic areas interspersed with small purpuric lesions beneath the mucosa When the process is fully developed the mucosal glands are involved and then the swollen mucosa may become granular in appearance In severe infection the entire mucous surface may become necrotic.

Material for culture is best obtained from swabbing the rectal lesions at the time of the endoscopic examination.

The leukocyte count varies from normal limits to 50,000 cells per cubic millimeter; usually there is a high percentage of neutrophils Erythrocyte counts vary; they may be high when dehydration is present and low when a mild secondary anemia exists in association with the chronic forms of dysentery.

The feces are examined for ova and parasites with particular reference to the presence of *Endamoeba histolytica*

DIAGNOSIS. The diagnosis of a particular etiologic agent as the cause of endemic acute diarrheal diseases can be made with certainty only in the laboratory by isolation of the etiologic agent or agents Cultures of the feces or material obtained by swabbing at the time of endoscopic examination are made After cultures are taken, chemotherapeutic or antibiotic agents should be given promptly. The physician knows that most of the patients suffering from acute diarrhea who come for attention have specific enteric infection due to some of the *Shigella* organisms The organisms which prevail in the United States rarely give rise to the severe bacillary dysentery usually described as endemic and epidemic in tropical climates.

Acute diarrhea caused by *Salmonella* cannot be differentiated clinically from that due to *Shigella* The former tends to give more fever, vomiting, greater abdominal tenderness and less blood in the stools A certain diagnosis must await laboratory findings (see *Salmonella* and salmonellosis, Chapter 17).

The features of an outbreak of an epidemic of dysentery are of diagnostic importance A sudden outbreak of severe dysentery is observed in staphylococcal food poisoning and in so-called sewage poisoning. Infections with enteric pathogens also occur as sudden outbreaks

Epidemics due to the *Shigella* continue throughout a period of several weeks The number of those ill with disease slowly or rapidly increases depending on the source from which the epidemic is disseminated and the sanitary control. The peak in incidence may be reached only after a month or more The decline in the number who succumb to the infection may be more rapid than the rise. An occasional instance of *Shigella* infection is observed for prolonged periods after an epidemic owing to convalescent and passive carriers infecting those about them Shigellosis is not attended by a septicemia

An epidemic of *Salmonella* infection begins in a period of 3 to 7 days, with a peak on the second or the third day

Highly selective mediums which permit growth of the enteric pathogens but inhibit growth of most of the nonpathogens are now available. Fecal specimens obtained by rectal swabs may be used for immediate direct inoculation of the selective mediums

Agglutination tests with the patient's serum cannot be interpreted with sufficient accuracy and speed to warrant the use of this procedure in diagnosing diarrheal diseases.

Acute Enterocolitis of Viral Origin. An acute diarrhea is a common manifestation of many systemic infections, bacteremia, septicemia or pyemia (see Chapter 17).

The acute enteritis due to bacteria or viruses may be divided into two large categories. (1) those due to an involvement of the stomach and intestines or intestines alone and (2) those which are part of a general infection or other systemic disease. In the second category the stomach and intestines or the intestines alone are affected secondarily.

The ingestion of partially decomposed, fermented, or putrefied foods accounts for many small epidemics of acute enteritis. The common agents which may give rise to infection from spoiled foods are the staphylococci, colon bacilli, *Clostridium botulinum*, and *Salmonella* which are not filtrable viruses

A disease of viral origin occurred in epidemic proportions in Philadelphia. The disease resembled the acute viral infection, white scours, which occurs in calves. This viral infection was characterized by diarrhea, nausea and vomiting. Results of bacteriologic examinations of the stools and pharyngeal secretions made by Reimann and his associates were negative. These investigators then resorted to experimentation on volunteers Broth garglings and suspensions of diarrheal stools were passed through a Mandler filter The resulting filtrates were nebulized. Twenty-one volunteers inhaled the nebulized stool filtrates In 11 of them diarrheal symptoms developed after an incubation period of less than 4 days. In 3 of the volunteers the diarrhea was accompanied by a mild nasopharyngitis Thirty-two volunteers inhaled nebulized filtered garglings; in 17 the diarrhea developed without nasopharyngitis. In 53 per cent of the volunteers who inhaled, typical viral diarrhea developed, as compared with only 9 per cent of the nonvolunteers, who acquired the disease during the same period of time from environmental exposure

Proved instances of dysentery due to viral origin as occurred in Philadelphia are lacking Influenza may cause abdominal cramps, diarrhea, nausea and vomiting. In contrast to the paucity of data, it is generally believed by many if not all physicians that viruses are potent influences for the initiation of intestinal disorders with dysenteric manifestations Indeed, many diseases which cause inflammatory changes in the stomach and intestines have their inception with acute diarrhea Often a patient who has any one of the following conditions. enteric tuberculosis, cholera, pyemia, septicemia, bacillary dysentery, a deficiency state, hypoproteinemia and severe anemia, congestive heart failure, hyperthyroidism, portal hypertension, chronic pulmonary disease, chronic intestinal obstruction, or embolic phenomena such as occur in rheumatic fever and bacterial endocarditis, or a patient in the terminal stage of nephritis (uremic states), or one who has malignant disease, or ulcerative colitis or terminal ileitis, will complain of having had a "virus dysentery" which started all of the trouble. It is well to know that the initial presence of an enteric virus is not necessary for the inception of any of these diseases If this fact is remembered, fewer diagnoses of viral dysentery will be made

Lymphopathia Venereum of the Rectum. This viral disease occurs in both men and in women. The adenopathies or buboes are the commonest manifestation of the infection in men The genito-anorectal form and rectal localization of the disease are much more frequently present in women than in men (see Chapter 7). The influence of race and color is not yet established, but the disease seems to be more frequent in the colored races than in whites.

The pathologic changes which lead to a rectal stricture are the important pathologic considerations here. According to Martin the perirectal and pararectal lymphangitis with marked lymphocytic infiltration finally becomes organized into dense fibrous tissue which produces stricture There is a great deal of connective tissue proliferation that seems to invade the muscular coats from the perirectal tissues.

It is the consensus that in women the rectovaginal and anorectal lymph channels are first affected and that then the perirectal lymph nodes also become inflamed and swollen Later, lymphatic occlusion and abscess formation ensue. This process is followed by ulceration, elephantiasis and fistulization The end result is scarring with rectal deformity and strictures

In some of those who have the disease there may be observed regional edema and

infiltration of the lymphatic structure of the dorsum of the penis which, when present with signs of other venereal infections, are pathognomonic of the coexistence of lymphopathia venereum.

After an incubation period of from 3 to 5 days there appears on the genitalia or in the orifices thereof a small herpetiform ulcer, papule, vesicle, or pustule (see Chapter 7).

Symptoms of rectal strictures develop without the patient having knowledge of any preceding manifestations. Because the rectal symptoms develop months or years after the buboes, and the course of the disease is so chronic, the stricture formation is probably a late phase of the infection

Rectal bleeding recurs daily for months or even years but rarely is the bleeding excessive. Little or no pain is experienced until the stricture develops. Mucoid seròpurulent or sanguinopurulent rectal discharge, watery diarrhea, and loss of appetite and of body weight are frequent complaints.

On examination the primary lesion of lymphopathia venereum is observed as a superficial ulceration on the external genitalia which may disappear soon or become a large, deep and extending ulceration If the ulcer forms on the upper two thirds of the vulva, inguinal or femoral lymphadenitis ensues There may be only one lymph node in the inguinal region enlarged with smaller nodes around it The enlarged node is tender Some time later a focal necrosis may occur and a small abscess follows. An extension of the necrosis to the surrounding superficial structures is manifested by ulceration and fistulization with fibrotic scarring

Skin eruptions associated with lymphopathia venereum were present in one third of Sonck's 400 cases The reaction is produced by sunlight, or by a hot steam bath. The primary lesion is a disseminated, punctate, reddish papular eruption appearing from one-half hour to 3 hours after exposure It is limited to the regions exposed to the sun's rays or to heat Desensitization occurs during spring or summer; however, the condition may last for 10 years

Sonck observed *allergic phenomena*, such as inflammation of the joints and eyes, erythema nodosum and rashes similar to erythema multiforme in association with lymphopathia venereum

There may be *ocular* manifestations of the disease Conjunctivitis may occur as a part of the infection of lymphopathia venereum. In the more severe infections abnormal visibility and tortuosity of the corneal nerves, increased opalescence of the cornea, blurred outline of the optic papilla, retinal edema, abnormal dilatation, tortuosity and a dark hue of the veins, ocular hypotension and retinal arterial hypertension are noted

On routine sigmoidoscopic examination when the infection is acute the mucosa of the rectum and the rectosigmoid is congested and bleeding, and the ecchymotic rectal mucosa is covered with blood clots and mucus In some patients there may be present macular, papular and vesicular lesions. The vesicular lesions contain yellow purulent contents These frequently ulcerate

In patients in the more chronic stage of the disease often no change is found except that of scarring of the mucosa in association with a smooth rectal stricture in the scar In other cases the proctologist may report that in association with the stricture the mucosa, both proximal and distal to the stricture, is reddened, edematous, granular, friable, bleeding, or thickened

The rectal stricture present late in the course of the disease tends to involve the rectal and the perirectal tissues extensively. The stricture is above the anorectal line, extending upward from about ½ inch to 4 inches (1.3 to 10 2 cm.). The caliber may admit the index finger, but is usually smaller. Vaginal examination may reveal the dense rectum The entire pelvis below the reflection of the pelvic peritoneum may be filled with dense indurated scar tissue

In instances of chronic infections there are emaciation, ocular changes, and

solar dermal eruptions. Conjunctivitis and allergic phenomena, such as erythema nodosum or rashes similar to erythema exudativum multiforme, are more rarely observed in the chronic forms of lymphopathia venereum. Edema, local or dependent, or both, may be present.

The diagnosis is made from the history, the physical examination and the positive reaction to the Frei test (see Chapter 7). Lymphopathia venereum is differentiated from factitial proctitis due to previous irradiation. It is separated from an ulcerative colitis by the history and by manifestations of the disease If strictures have resulted from trauma or physical agents, such as hot enemas, the history will differentiate

It is surprising that the opening in a strictured rectum, although extremely small, is capable of carrying on fair bowel function often for many years.

Diseases of the Colon Due to Higher Animal Parasites. The Class Sarcodina. This class, comprising unicellular animals that form pseudopodia, includes several orders and many families Most of the parasitic species in man are included in the order Amoebida and the family Endamoebidae.

The Parasitic Amebae of Man. At least 4 genera and 6 species of amebae of the family Endamoebidae live in man. These are· genus *Dientamoeba*, species *Dientamoeba fragilis*, genus *Endamoeba*, species *Endamoeba coli*, species *Endamoeba gingivalis*, and species *Endamoeba histolytica*, genus *Endolimax*, species *Endolimax nana*, and genus *Iodamoeba*, species *Iodamoeba buetschlii* However, *Endamoeba histolytica* is the only known pathogen in man.

Immunity The resistance of the host is the chief factor in determining the occurrence of clinical disease in amebic infections. However, strains of *Endamoeba histolytica* vary in virulence. Evidence of racial immunity is inconclusive, although the white races in the tropics seem more susceptible to clinical disease than the natives Continued exposure to heavy infections may overcome resistance. The relation of the carrier state to immunity is not clearly defined. Precipitins and complement-fixing antibodies have been demonstrated in the blood

Incidence Surveys which have been made to determine the prevalence of parasitic amebae in man have shown that the incidence of infection of these amebae is highest in the tropics and subtropics Thus the incidence, to a large measure, depends on geographic location.

Surveys for the incidence of amebic infection are not made in districts where these infections are not common It is therefore appropriate to say that in some districts of the United States of America amebae are common, and in others, rare

1. *Endamoeba histolytica.* Some authorities prefer the generic name *Entamoeba* to the approved *Endamoeba* Confusion in nomenclature has produced many synonyms. Among the more prominent are *Amoeba coli*, *Entamoeba dysenteriae*, *Entamoeba histolytica*, *Entamoeba tetragena*, *Entamoeba hartmanni*, *Loeschia histolytica* and *Endamoeba dysenteriae*.

The diseases caused by amebic infection are amebiasis or amebic dysentery, and amebic abscess of the liver

The ameba carrier state is chronic, its duration being measured in months rather than in days and weeks as it is in bacillary dysentery

The sources of infection are the carrier or asymptomatic contact and the chronic convalescent patient who are passing infective cysts. In acute dysentery encystment does not occur, either because conditions for cyst formation are unfavorable or because the trophozoites are discharged too rapidly to permit encystment. Hence patients who have the disease in acute form are not important sources of infection, since the trophozoites rapidly perish outside the body, and are destroyed by the gastric secretions if they reach a new host. The mature cyst is apparently the infective form

Endamoeba histolytica may be observed in the feces in three morphologic stages: (1) the trophozoite, (2) the precystic and (3) the cystic.

Life Cycle The life cycle of *Endamoeba histolytica* is comparatively simple The

formation of infective cysts in the large intestine is followed by their passage in the feces, their extracorporeal existence and their ingestion by a new host.

When amebae are ingested by man, the mature cysts pass unaffected through the stomach. In the lower part of the small intestine the cyst wall disintegrates, liberating a four-nucleated ameba, which divides ultimately into eight small trophozoites These small active amebae move downward to the large intestine, where they invade the mucosa, submucosa and muscular tissues of the intestinal wall, aided by the action of their cytolytic ferments and by their ameboid movements. From the intestinal wall the amebae may spread to secondary sites They may reach the liver by way of the portal vein, thence by the blood to the lungs, brain and other organs, where they multiply in the tissues.

The pathologic lesions of amebic infection of the intestinal wall are of three types: (1) early minute nodular flasklike cavities, (2) irregular crateriform ulcers with ragged edges and (3) communicating sinuses between adjacent ulcers

The primary lesions are largely confined to the large intestine, a few may be situated in the lower part of the ileum near the ileocecal valve The lesions are often scattered throughout the colon. Isolated infected regions of the colon are situated in the following order of frequency cecum, ascending colon, rectum, sigmoid and appendix

The secondary lesions usually occur in those who have active primary lesions However, hepatic abscesses have been found in patients who gave no history of dysentery Chance determines the establishment of a secondary infection

In the liver the amebae first cause hepatitis and then dissolve the hepatic cells, producing single or multiple abscesses, usually in the right lobe The living amebae are continually invading the marginal tissue As the abscess increases, its wall thickens and the contents become a viscid chocolate-colored or reddish mass of hepatic cells, erythrocytes, bile, fat and other products of tissue dissolution There is usually only one abscess, but it may reach a large size and even rupture into the peritoneum or pleura Secondary bacterial infection produces purulent changes

About one half of the dysenteric patients who come to necropsy show major or minor involvement of the liver since the presence of amebae in the liver does not invariably mean a hepatic abscess Once within the circulation, amebae may be carried from the liver to any organ of the body, such as the brain, lungs, and spleen, there are instances, but not without question, of the involvement of urinary bladder, testes, epididymides, lymph nodes, skin, bones and joints

SYMPTOMS The ordinary state of infection is an equilibrium between parasite and host, and the typical infected individual is an asymptomatic carrier The contact carrier maintains a low-grade infection, but whenever his resistance is lowered, he may succumb to the disease The convalescent carrier has recovered from dysentery, but is subject to clinical relapse Clinical dysentery develops in about 1 of 10 infections The incubation period varies from a few days to months and even years, since clinical dysentery may develop at any time in asymptomatic carriers. The period of incubation in the severe and highly fatal Chicago epidemic of 1933-1934 was less than 1 week in 6 7 per cent of 495 cases, less than 4 weeks in 64 7 per cent (mean 12 days) and less than 8 weeks in 91 per cent.

The infected person does not manifest symptoms, but there is often an awareness of slight discomfort The patient may have mild toxemia, or may suddenly be seized with dysentery

Acute dysentery varies in severity from the rare fulminating illness with marked toxemia to the mild attack with spontaneous recovery The onset may be sudden with acute abdominal pain, nausea, vomiting, fever (temperature 100 to 102 F, 37 8 to 38 9 C) and occasionally chills; more often it is insidious and is preceded by attacks of mild or severe diarrhea. At the height of the attack the patient may have 15 to 20 or more daily movements of blood, mucus and, in severe cases, bits of necrotic mucosa

The patient who has *chronic dysentery* manifests symptoms of dysentery only during exacerbations. At all other times the bowel movements are normal except for the usual constipation or minor intestinal irregularities that almost everyone has In

4. *Trichomonas hominis*. All intestinal trichomonads, irrespective of whether they possess three, four, or five anterior flagella, are designated here as *Trichomonas hominis*. At least three forms have been described as distinct species, *Trichomonas fecalis*, *Trichomonas hominis* and *Pentatrichomonas ardin delteili* (see *Trichomonas vaginalis* in Chapter 7).

Trichomonas hominis, probably nonpathogenic, causes intestinal trichomoniasis

Trichomonas elongata (*Trichomonas buccalis*) is nonpathogenic to man.

The Superfamily Oxyuroidea (Nematoda). The members of the superfamily Oxyuroidea are small, pin-shaped, meromyarial nematodes parasitic in the large intestines of vertebrates The two species which occur in man, *Enterobius vermicularis* and *Syphacia obvelata*, belong to the family Oxyuridae

1. *Enterobius vermicularis* This parasite causes *pinworm infection* (enterobiasis, oxyuriasis). Man is the only known natural host of *Enterobious vermicularis*.

Of cosmopolitan distribution, *Enterobius vermicularis* is a small, round worm which inhabits the rectum, bladder and the adjacent portions of the large intestine of man.

Oviposition does not occur until the female worm is stimulated by contact with air, the ova are not commonly laid in the intestine. The female releases her hold on the intestinal mucosa, and either is passed in the feces or migrates at night from the anus and crawls actively in the perianal and perineal regions, even entering the vagina or more rarely the bladder The ova are expelled in masses and are left behind as the worm advances from place to place over the perianal and genitocrural folds Occasionally the female worms cause itching If the worm dries, it explodes with showers of ova

Outside the host an infective larva develops within the shell in a few hours The hands, particularly beneath the fingernails, become contaminated with adherent ova through handling the perianal regions Thus infective ova are readily transferred to the same or another host either directly by hand to mouth or indirectly through food and drink The ova that adhere to night clothes and bed linens may also be transmitted by the hands.

Upon ingestion the embryos are liberated in the duodenum

The presence of the parasite is suspected clinically in children who manifest intense nocturnal perianal itching Diagnosis is made by finding the adult worms or ova Often the first evidence of infection is the discovery of the adult worms in the feces, particularly after enemas In the feces the worms must be differentiated from fly larvae The ova are seldom found in the feces even with concentrative methods Ova are frequently obtained from fingernail scrapings.

Diseases of the Colon Due to Trauma, Physical Agents and Static Abnormalities. Rupture of the Colon and Rectum. Spontaneous rupture of the colon probably does not occur unless there is disease of the intestinal wall When rupture does occur, it is due primarily to a rise in intraluminal pressure produced by air or water, foreign bodies, external violence, extracolonic diseases, or trauma to the wall of the bowel.

Perforation of the bowel during the course of sigmoidoscopic examination may not be suspected until the signs of diffuse peritonitis become manifest In other instances of tears the wound may be seen in the bowel, usually at or near the rectosigmoid. The tear is often manifested by a rush of air inward during expiration as soon as the hole is made.

If there is evidence of trauma, there usually is a history of sudden onset of pain of great severity, with the rapid development of the signs of shock and peritonitis The signs of shock—boardlike rigidity, absent peristalsis and, perhaps, evidence of pneumoperitoneum—are present In some instances the symptoms and signs of peritonitis may be delayed from a few hours to a day after the wound in the bowel has occurred

A roentgenologic examination of the abdomen and the demonstration of pneumoperitoneum are diagnostic of a perforated, air-containing viscus.

As soon as a diagnosis of rupture of the colon is made, operation must be undertaken at once, delaying only for preparation of the patient and treatment for shock. The prognosis is always grave.

Foreign Bodies in the Intestine and Colon. Many foreign bodies, especially such small objects as fish bones, tacks, bits of glass and parts of oyster or egg shells, are ingested unknowingly.

The desire to conceal objects or to destroy incriminating evidence may lead individuals to swallow foreign bodies or introduce them into the rectum Instances in which drug addicts have concealed narcotic vials in the rectum are common.

During the course of examination or treatment an instrument may slip into the rectum or be swallowed. Stomach tubes may be completely swallowed or metal tips become dislodged in the stomach Rectal thermometers and nasal suction tubes are occasionally recovered from the sigmoid or the rectum.

A foreign body may remain in the lumen of the bowel for years, giving rise to no symptoms Swallowed foreign bodies may be held up at those sites in the alimentary tract which are normally narrow, fixed, or angulated; these sites include the pylorus, duodenum, ileocecal valve, hepatic and splenic flexures, rectosigmoid and rectum

The symptoms of foreign body in the intestine and colon depend on the site of lodgment of the object, the character and size of the object, and the presence or absence of complications

The history is important but often is unreliable in diagnosis of a foreign body in the colon or rectum Frequently the patient does not know that a foreign body has been swallowed Patients who have mental aberrations from anesthesias, hypnotics, or narcotics, or those who are psychotic may swallow foreign bodies.

Foreign bodies lodged in the cecum may simulate appendicitis. The anal crypts may act as repositories for small foreign bodies, severe proctitis and even abscess may result

If the foreign body is irritating or of a type capable of causing lacerations of the gastrointestinal mucosa, a severe gastroenteritis may ensue. Large foreign bodies impacted in the rectum may cause complete obstruction of the bowel associated with abdominal swelling, rectal pain and bleeding, and tenesmus

The clinical findings on examination may resemble those of an abscess, appendicitis, diverticulitis, general peritonitis, intestinal obstruction, proctitis, or a malignant mass

Digital examination is an important procedure when objects are suspected of being in the rectum If the object is high in the rectum, proctosigmoidoscopic and roentgenoscopic examinations are valuable The barium always is administered as an enema

The diagnosis is made by finding the foreign body

The complications of foreign bodies in the intestinal tract are hemorrhage, laceration of the bowel, perforation with peritonitis or abscess formation, fecal, rectal, rectovaginal and rectovesical fistulas, cryptitis, chronic granulomas, fecal impactions and intestinal obstruction. Some of these complications may occur as the result of attempts at removal

Obstruction to the bowel may occur when the foreign body is large or when it acts as a center for the deposition of a fecal concretion, such as occurs in obstruction by a large gallstone

A foreign body in the intestine or rectum which remains fixed and will not pass on should be removed surgically

Factitial Proctosigmoiditis. When irradiation therapy is necessary in the rectal or genital regions, it is well to tell the patient and the family of the possibly serious effects which may follow the use of radium or roentgen therapy. If this is done,

excessive terms will not be required for naming the possible complications (see Chapter 19).

Bleeding from the rectum may appear at any time during the period of the radium treatment to 6 years after irradiation therapy. *The rectal bleeding is increased* by defecation, rectal examination, or instrumentation. The rectal bleeding may be uncontrollable, so that the patient bleeds to death. A frequent and very urgent desire to defecate is commonly present during the stage of active proctitis and bleeding Pain in the rectum may be severe and may radiate to the sacrococcygeal region and to the thighs and groins The pain, like the bleeding, is intensified by defecation and by standing or walking. Fever and fistulous communications with the vagina and urethra are severe complications which often lead to confinement in bed and emaciation and finally death

The general examination in those who have had roentgen rays or radium applied to the skin reveals areas of induration, telangiectasis and pigmentation of the sites of exposure to the rays

On rectal examination of those who have been treated for carcinoma of the cervix, there may be a palpable induration or a hard tumor on the anterior wall of the rectum In some there is an ulcer with a crater, with or without a surrounding mass Palpable annular strictures are common. These strictures are often present in those who have rectovaginal, rectovesical, perineal or perianal fistulas and a recurrence or an extension of the malignancy.

The proctologist may report that the mucosa appears reddened and edematous and bleeds easily following the slightest trauma Later the mucosa is described as indurated and showing telangiectasis.

Fecal Impactions of the Colon and Rectum. Fecal impaction is commonest in the rectum, but it may occur in the sigmoid or cecum and even in the transverse colon. There is usually one impaction which increases proximally from the initial impaction

Some persons regularly pass several days without an evacuation of the bowel. The addition of excessive tension and fatigue plus insoluble medications, bulk-forming cathartics and undigested food particles may result in a great mass of feces accumulating in the colon or rectum before distress occurs.

Other persons do not yield to the desire to defecate and as a consequence there is a gradual dilatation of the rectum, with eventually a loss of the defecation reflex. Under these circumstances the patient becomes unaware of the presence of feces in the rectum until a very large fecal mass accumulates, and impaction may be the consequence

Often those who have a large part of the body enclosed in a cast, or elderly patients who are confined to bed, have fecal impactions

Fecal impactions are prone to follow barium meals if the barium is not emptied from the bowel.

Anal lesions or anorectal manipulations or operations which cause pain on defecation may predispose to impaction of feces

Pregnancy, pelvic and large abdominal tumors, and ascites may act as predisposing causes of fecal impaction. This complication of constipation is perhaps most likely to develop in multiparae and aged individuals in whom the perineal and pelvic supports are relaxed.

Megacolon is an effective but a rare cause of impaction

The desire for defecation is always the most persistent and severe symptom. Often the first and sometimes the most persistent symptom of an impaction may be what the patient considers to be a diarrhea This paradoxical diarrhea is in reality a tenesmus with discharge of small amounts of mucus and feces. The abdominal pain or cramps which are present in the beginning often subside or become intermittent after the impaction has existed for a day or two

Stercoromas can achieve great size, causing swelling of the abdomen and large, easily palpable masses. The commonest palpable abdominal tumor is constituted of

the commonest material in the abdomen—feces On palpation of the abdomen a stercoroma feels much harder than a carcinoma, and the tumor is freely movable. Constitutional symptoms, particularly anemia and loss of body weight, are usually absent in patients who have stercoroma When a stercoroma is felt digitally, it should be broken up into several parts

Fecal impactions in the rectum are easily diagnosed by means of digital examination. When the impaction is in the lower part of the sigmoid, direct visualization by means of the sigmoidoscope often is possible Fecal impactions or stercoromas in the transverse colon or in the cecum may not be easily diagnosed roentgenologically.

The most serious complication of fecal impaction is perforation of the wall of the bowel with general peritonitis ensuing or abscess formation.

Melanosis Coli. The pigments in melanosis coli are melanins or epithelial pigments The entire colon may be involved, with an abrupt demarcation and ending at the ileocecal valve Pigmentation in some patients is most marked in the cecum and ascending colon, and in others is more intense in the descending colon.

The incidence of these pigmented bowels is not known, but the condition is not rare. In some instances of extreme pigmentation the degree of coloration is the same throughout the rectum and sigmoid The condition occurs between the ages of 30 and 60 years, in both men and women and in both Negroes and whites

Obstinate constipation is present and often is the reason that the patients seek medical advice Cascara sagrada is taken either alone or in combination with alophen, aloin, or rhubarb by many of these persons. Melanosis coli occurs, however, in those who have not taken cascara sagrada

Melanosis coli cannot be held responsible for any known complaint or symptoms It does not predispose to malignancy.

Diseases of the Colon Due to Unknown Causes. *Chronic Ulcerative Colitis.* This disease is called also colitis gravis, chronic suppurative colitis, idiopathic ulcerative colitis, nonspecific ulcerative colitis and thrombo-ulcerative colitis. This is not a common disease

The cause is unknown There are certain factors which seem to be of etiologic importance but cannot be proved These are the so-called constitutional, infectious, allergic and psychogenic factors

The constitutional factors which might be of etiologic importance comprise the possible intrinsic systemic abnormalities, such as those of endocrine glands, and the allergic, psychogenic and neurogenic disturbances. Endocrinal influences or metabolic states, however, seem to play no part in the etiology of ulcerative colitis The conditions requisite for diagnosis of an allergic state are not fulfilled by ulcerative colitis unless the patient accidentally has both conditions

The course of any chronic disabling disease is affected by psychogenic factors [illegible] Before the present [illegible] cians were aware [illegible] their great influ- [illegible] opinion arise in regard to the order of appearance of the emotional disturbances and the ulcerative colitis On this point and, consequently, on the etiologic importance of emotional [illegible]

[illegible] support either of these as possessing great etiologic possibilities

[illegible]

reac [illegible]

The [illegible]

The [illegible] between bacillary dysentery and ulcerative colitis are the variation in onset and duration and the lack of evidence of infectivity or contagion in ulcerative colitis

The terms colitis gravis, nonspecific ulcerative colitis and idiopathic ulcerative colitis are used to describe a diffuse hyperemia, granular in appearance, of a segment or all of the colonic mucosa which progress to ulceration and scar formation

In the early stages of the disease there are hyperemia and hemorrhages under the mucosa and submucosa and ensuing shallow erosions and deep ulcerations The ulcerations are irregular in size and location. In the rectum the ulcers tend to coalesce, denude and undermine the mucosal surface and leave mucosal tags. As the disease becomes more chronic, there are polypoid and proliferative changes. The muscular layer is thickened from edema A replacement of the muscular layer by inflammatory tissue ensues with contraction of the scar tissue which produces narrowing deformities of the lumen of the bowel and shortening of its length Strictures, perforations, hemorrhages and obstructions are common

Ulcers situated proximally to the rectum in the sigmoid, descending colon, transverse colon and ascending colon tend to be elliptical with their long axes parallel to the long axes of the bowel Circular groups of ulcers may follow the course of the muscle fibers Often there are thinned spots of the intestinal wall which may perforate Likewise there are hyperplastic areas of mucous membrane which have an ample blood supply and participate in the formation of pseudopolyps.

The entire rectum and colon are frequently involved by the disease Occasionally the distal portion of the ileum is affected along with the colon One or more segments of the colon may be involved without disease of the rectum. When only parts of the colon are involved, the condition is termed regional or segmental ulcerative colitis If only the rectum and the sigmoid are involved, this is termed proctosigmoiditis On the basis of segmental distribution of ulcerative colitis Bargen has classified the disease accordingly into four groups These groups serve mainly as a basis for the study of many cases

Ulcerative colitis is cosmopolitan. It is less prevalent in the warmer portions of the United States of America than in the northern sections

The onset of ulcerative colitis may occur at any age but usually before 40 years There are no sex preferences It shows no house, community or family incidence. The presence of more than one case of ulcerative colitis in the same family is unusual, but there are exceptions.

SYMPTOMS. The onset is characteristically insidious and may be unassociated with diarrhea In rare instances constipation may prevail throughout the course of the disease In many cases, however, the passage of 3 to 5 stools a day may constitute the first symptom, and the appearance of bloody mucus on the outside of the stools is an almost constant early symptom In some instances the first known symptom of the disease may be abrupt, with diarrhea, and in some without the gross appearance of blood in the feces In the onset of the acute fulminating type of the disease the patient may have almost continuous liquid evacuations, composed almost entirely of blood, pus and mucus In these the involuntary passage of the bowel movement is common

Abdominal pain, colicky or crampy in type, and often confined to the lower abdominal quadrants, almost always accompanies the bloody dysentery. The pain occurs with the desire for defecation and is relieved in some, while in others it is made worse, by a bowel evacuation Rectal tenesmus is constant and fatiguing and afflicts all of those who have rectal involvement and frequent bowel movements The irritation of the anus by the frequent bowel motion may create fissures and if so the anal pain becomes severe and fatiguing.

Anorexia, fullness, nausea, epigastric discomfort and often vomiting are commonly present. Besides their importance in the addition to the patient's discomfort, [illegible] normal

[illegible]

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Chronic ulcerative colitis is characterized by remissions and relapses of symptoms The recurrences are usually in the form of acute exacerbations of the disease

However, there are chronic forms of the disease which are continuous Relapses of chronic ulcerative colitis seem to result from (1) infection in the upper part of the respiratory tract, (2) dietary indiscretions and partaking of alcoholic drinks, (3) fatigue, operative procedures, gestation, generalized or localized infections and (4) emotional or psychic disturbances.

The symptoms of chronic ulcerative colitis may be changed on any day from the time of its inception until death by the appearance of a complication. The complications are numerous, and in view of the seriousness of the disease, all complications likewise are serious

A *fibrotic constriction* of the lumen of the diseased colon is one of the commonest complications of ulcerative colitis Stricture may develop in any segment of the colon, but seems to occur most often in the rectum These strictures are often manifested by symptoms of obstruction to the emptying of the colon or rectum.

Massive hemorrhage is common However, more commonly there is prolonged and profuse bleeding. Hemorrhages are, therefore, an important complication of this disease

Subacute or chronic *slow perforations* may produce an extensive tissue reaction without actual abscess formation but may terminate in formation of abscess and fistula.

The infiltration of the tissues due to either perforation or permeation may result in local *abscess formation* Such a collection of pus may drain into the rectum with *sinus formation*, it may point and drain outside the anus with resulting *fistulization*, it may drain through the vagina (rectovaginal fistula), or it may drain into the bladder (rectovesical fistula) Occasionally a large pelvic abscess or localized peritonitis occurs This complication may prove serious and may require drainage. However, the surgeon should be prevailed on not to be hasty to lance an apparent abscess, for the abscess may open elsewhere despite the surgeon's efforts.

During the course of ulcerative colitis and in acute exacerbations, usually while the patient is confined to the bed, *involvement of the joints* is frequently observed. The articular symptoms improve with improvement of the colitis and recur with exacerbations of the colonic disease Arthralgia and myositis in association with ulcerative colitis are common, particularly after prolonged high fever. Such involvement of joints perhaps is no commoner among patients who have chronic ulcerative colitis than among patients who have any other chronic disease which is characterized by the presence of fever, pain and confinement to the bed. The pain is so severe in many of these patients that they lie quietly except when disturbed by bowel movements

EXAMINATION The skin of a patient who has ulcerative colitis is usually normal except during periods of exacerbations when fever and dehydration are present. The skin is then dry and loose because of loss of water and electrolytes and subcutaneous tissues Evidences of vasomotor instability may be prominent.

The condition of a patient who has been seriously ill or who has sitophobia is often complicated by nutritional deficiencies In these patients changes in the skin [illegible]

[illegible] recur

[illegible] esions, described variously as phagedenic ulcers, phagedenic pyoderma, chronic burrowing ulcer and pyoderma gangraenosum, occur These lesions may follow surgical operations and the prolonged fever in association with ulcerative colitis. Although rare, phagedenic lesions are extremely serious.

Loss of weight, pallor, and weakness are evident in most of those who have had the disease for a long time (months, sometimes years).

The tongue, mouth and eyes rarely show changes associated with nutritional deficiency or suggestive of allergy.

The terms colitis gravis, nonspecific ulcerative colitis and *idiopathic ulcerative colitis* are used to describe a diffuse hyperemia, granular in appearance, of a segment or all of the colonic mucosa which progress to ulceration and scar formation.

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Anorexia, fullness, nausea, epigastric discomfort and often vomiting are commonly present. Besides their importance in the addition to the patient's discomfort, they are responsible for inability to eat and thus for difficulty in maintaining normal nutrition The loss of body weight and strength is related more to severity of these symptoms than to the severity of the disease unless there is prolonged high fever

Chronic ulcerative colitis is characterized by remissions and relapses of symptoms The recurrences are usually in the form of acute exacerbations of the disease

oped disease the mucosa becomes red and edematous, presenting a characteristic pitted, granular appearance. Usually there is a constant oozing of blood from the surface while the examination is being made.

Roentgenologic study after a barium enema has been given may be considered as an extension of the endoscopic examination and necessary for diagnosis of the extent of the disease.

The prognosis for life, despite the many complications, is generally good. The mortality rate is greatest during the first year of the disease and decreases thereafter. The expectation of life improves with the passage of time. The prognosis for cure is totally bad. No one can ever be sure that the disease has been cured as long as the colon remains in the abdomen

In those whose symptoms are not acute in the beginning, the disease is likely to continue as a subacute or chronic form, or to disappear entirely. Prognosis is poor in those who have a fulminating or a chronic continuous type of the disease. In those in whom the disease had an insidious mild onset, those who have definite remissions and relapses of symptoms, and those in whom the disease remains confined to the rectum or rectosigmoid, the prognosis is good, and many are able to adjust their lives accordingly That is, about 3 of every 4 patients should be rehabilitated for varying periods of time, none are ever cured medically. Some recover spontaneously

A free perforation of the colon is not an indication for operation, for suturing of the diseased bowel is impossible Carcinoma and stricture causing obstruction require surgical treatment Some severe perianal and perirectal infections progressively extend until the fecal current must be diverted Polypoid hyperplasia is not an indication for operation If an adenomatous change in the polypoid tissue is demonstrated on histologic study, operation should be advised

If surgical intervention is advised, it seems that the practicable procedure is ileostomy and colectomy by stages.

Tumors of the Colon and Rectum. ***Benign Tumors.*** Many of the benign lesions of the colon are polyps The terms polyp and polypous refer to a projective growth from a mucous surface They designate a form or shape of a lesion without regard to histologic structure

Certain polypous or polypoid lesions which appear in the colon and rectum are congenital in origin These lesions comprise polyps, teratomas, dermoid cysts, enterogenous cysts, angiomas, lymphangiomas and neurofibromas

In the immediate development of the *acquired* polypous or polypoid lesions of the colon and rectum there are certain factors which appear to be instrumental: hereditary predisposition to grow the tumors, primary epithelial hyperplasia, subsequent chronic irritation, inflammation, and finally primary subepithelial change

Polyps. The common type of polyp of the colon and rectum is an adenoma. However, it is incorrect to assume that a polyp is an adenoma until histologic study has proved it so

Erdman subdivided colonic polyps (adenomas) on the basis of their clinical behavior, etiology and histologic appearance into (1) the adolescent (congenital, disseminated) type and (2) the adult (acquired) type This subdivision is adequate for clinical description

In about one half of those who have multiple polypoid lesions of the bowel there is a distinct *familial disposition* indicating a factor of morbid heredity. Probably without

Fever is present with each acute exacerbation of the disease. In some patients there is often a continuous low grade of fever over long periods The temperature may rise to 103 or 104 F (39.4 or 40 C) each day for several weeks and in some for months, subsiding only to recur again.

On abdominal examination tenderness, usually generalized throughout the abdomen, is always present Some distention of the abdomen may be present. The results of palpation of the colon often are not significant. Rarely is the liver or the spleen palpable

Rectal examination and digital palpation of the mucous membrane often do not reveal any abnormality Edema and strictures may be felt. Polyps or carcinoma may be palpated if present The coarse, granular changes in the mucosa described by the endoscopist usually cannot be palpated Determination of the presence or absence of fistula of the rectum or the vagina can be made with aid of good history and light at the time of digital or endoscopic examination

The sigmoidoscopic examination reveals the granular, ulcerative, hyperemic appearance of the mucosa and the degree of contraction of the lumen, strictures, fistulas, fissures, and in some instances pseudopolyps The roentgenologic examination reveals the abnormalities in the sigmoid and the rest of the colon

Polyps and pseudopolyps are commonly found The pseudopolyps may have the appearance of genuine polyps Pseudopolyps seem to arise from shreds of mucous membrane which have a sufficient blood supply to remain alive and grow after being torn loose on two or three sides from the submucosa of the bowel and regions of hyperplastic mucosa which may grow until a polypoid mass is formed These are diagnosed by means of sigmoidoscopic and roentgenologic examinations *Pseudopolyps are differentiated from true polyps by microscopic examination of sections of the polyp*

The detection of carcinoma in chronic ulcerative colitis is made by digital or endoscopic examination of the rectum, or roentgenologic study of the colon after *barium enema Histologic study is required to confirm this diagnosis*

Free perforation with generalized peritonitis is rare in ulcerative colitis Perforation occurs in the extremely acute fulminating forms of colitis and in association with stricture formation Diagnosis of free perforation is based on the presence of an *acute peritonitis*

Measurable hepatic dysfunction rarely accompanies ulcerative colitis

Amenorrhea is the rule during the stage of activity of the disease When the disease begins in childhood, sexual development may be retarded and varying degrees of infantilism result.

Complete blood counts and hemoglobin determinations reveal presence or absence of anemia Many patients who have ulcerative colitis are anemic The degree of anemia is dependent on the amount of blood lost and the degree of iron deficiency. The total and differential leukocyte counts are frequently normal even during severe exacerbations of the disease. Leukocytosis may be present when complications arise

DIAGNOSIS. Sigmoidoscopists are in essential agreement that the following appearances of the mucous membrane of the rectum and rectosigmoid prevail in the early stage of chronic ulcerative colitis, and that when present these findings are diagnostic: The mucous membrane may be reddened in appearance. Application of a cotton swab may cause an elevation of the membrane In other instances the membrane has a granular appearance and may show a few fine bleeding points A mottled discoloration due to petechiae connected by a fine weblike network may be present. As the disease advances, there is a general hyperemia and the mucosa appears swollen After the surface is swabbed, it appears granular and there are bleeding points. Ulcerations may or may not be present. In instances of fully devel-

¼ to ½ inch (0 6 to 1 3 cm.). However, very large polyps may be present without discomfort.

About one fourth of all patients who have the disease complain of some form of abdominal distress. The discomfort varies widely in situation, character and severity. It is a cramplike pain which extends across the midsection of the abdomen and which is increased during and after bowel movements

Inflammation or ulceration often is present The development of characteristic ... When ... h very ... usual

A polypoid lesion may attain sufficient size to occlude the lumen of the bowel or it may so interfere with normal peristalsis as to cause intussusception. Intestinal obstruction may therefore be the reason for the patient to seek relief, and the polyposis is discovered at the time of surgical operation Frequently the obstructive phenomena occur in acute short-lived episodes which disappear spontaneously.

Pedunculated rectal growths may be extruded through the anus and on rare occasions the polyp may be spontaneously expelled There are records of patients who passed from the rectum the only polyp present Usually another polyp will grow in the same place at a later date

Examination Polyps, even small ones, under favorable conditions may be palpated The most favorable site for the palpation of a polyp is on the posterior surface of the rectum over the sacrum

When polyps are brought into view by the endoscope, or when their relief is depicted on the roentgenogram by contrast media employed by the roentgenologist, every conceivable variation in size and shape of polypoid lesion may be present, ranging from small excrescences on the mucous surface to large pedunculated masses The polyps may be widely disseminated over the luminal surface of the colon, there may be aggregations of polyps limited to one or more segments, often to the rectum or perhaps to a flexure, or there may be one polyp in the entire colon, or a few single polyps in the rectum

The status of a given polypoid lesion, whether *benign* or *malignant*, can be determined only by biopsy and histologic study The size or shape of a lesion is not significant The malignant status of the polyp may be evaded by reporting it as an adenocarcinoma in an adenoma The gross appearance of polyps which have undergone cancerous transformation often reveals ulceration, nodular irregularity, fixation, or induration There is much evidence which strongly favors the close relationship of polyposis to cancer Polyps are often found in carcinomatous colons

Diagnosis In the diagnosis the hereditary or familial features are obtained from the history. In patients who have the heredofamilial variety of polyps, rectal palpation may be diagnostic

... nosis is certain when a polyp has been examined microscopically The prognosis depends on complications, since the complications are the same in both the adolescent (congenital, disseminated) types and the adult (acquired) type

Lipomas Lipomas constitute the second commonest benign tumor of the gastrointestinal tract Despite this incidence, lipomas of the intestines are rare. They occur more frequently in the colon than elsewhere and they are somewhat commoner in women than in men.

Symptoms are commonly absent Intussusception occurs in about one third and bleeding in about one fourth of the patients who have any symptoms

individuals, representative of 5 generations of one family of German extraction, who have or have had hereditary and familial polyposis of the colon. In all of these the symptoms occurred before 40 years of age and there has been no sex preference

In many young patients no such evidence of morbid heredity is present In some there may be a limited familial incidence. One or two members of the family may be known to have had polyps of the rectum or colon However, about one half of those who have polyposis cannot present any genealogic evidence of polyposis.

Acquired polyps of the colon generally occur in older patients than those affected by congenital polypoid disease Polyps have been encountered in persons of ages ranging from 16 to 87 years; the most frequent occurrence is in persons in the fifth and sixth decades. In the large bowel they are situated, in order of frequency, in the cecum, ascending colon, sigmoid, transverse colon, rectum, and descending colon The polyps may be present singly or multiply or may occur profusely in segments of the colon

The actual incidence of these lesions may be at least partially appreciated from the data accumulated from studies made by Jackman and Mayo "In a series of 2,784 necropsies done at the Mayo Clinic in the five-year period from 1935 to 1939 inclusive in cases in which the patients had died of some other condition not related to the colon, 14 7 per cent of the 1,757 males in the group and 9 0 per cent of the 1,027 females were found to have polyps of the large intestine. Bear in mind that this study took in all ages from newborn to the age of 90 years. The peak incidence was found in persons who were in the age group from 60 through 69 years, in this group 26 4 per cent of 421 men and 15 4 per cent of 195 women had polyps. It could well be assumed that had these patients not succumbed to some other disease, the polyp would eventually have developed into carcinoma "

Polyps are to be found with surprising frequency in colons which are already the seat of carcinomas Also it seems that there is an increased incidence of polypoid lesions in association with chronic ulcerative colitis aside from the so-called pseudopolyps

Symptoms Patients who have uncomplicated polyposis may not be ill. The abdominal examination does not reveal the presence of any abnormal condition in most of those who have heredofamilial forms of the disease until complications are present

There is considerable evidence to indicate that polyps of the rectum and colon may be present for a long time without producing symptoms For instance, McKenney presented evidence which suggests that the lesions in congenital polyposis are present at a very early age and progressively grow before sufficient symptoms are present to require an examination

As many as half of the patients who have multiple polypoid lesions of the colon may have had symptoms for 10 years or longer before the diagnosis is made The duration of symptoms varies from 1 day to 7 years, in the majority, however, from 6 months to 3 years

The symptoms which may be produced by polyps are like those for all of the benign tumors of the colon They are dependent on several factors the size, the situation, and the number of polyps and the presence or absence of complications

Blood in the stools is complained of by two thirds of all patients who are found to have one or more polyps of the rectum and colon As a rule, the bleeding is [illegible] more than is present in many cases [illegible] ents discovered to have polyps will [illegible] aracterized by acute exacerbations [illegible] Like the bleeding, it is inconstant, intermittent and not severe, it may be accompanied by pain but often the diarrhea is the only symptom .

[illegible] and urgency on defecation with an unsatisfactory feeling of incom- [illegible]

spread has extended to the extrarectal tissues (type B Dukes); and (3) those in which metastasis is present in the regional lymph nodes (type C, Dukes). This classification supports an observation, often expressed by William Worrall Mayo, that tumors which project toward the lumen are more benign, whereas deeply excavated ulcers in tumors which grow away from the lumen are more malignant

Broders' classification is an estimate of the degree or grade of malignancy based on the rate of growth; tumors are divided into four groups depending on the percentage content of differentiated cells as compared with undifferentiated cells observed microscopically (degrees of anaplasia), grade 1 indicating the lowest degree of malignancy and grade 4 the highest. About 3 of every 4 carcinomas of the colon are of Broders' grade 1 or 2.

Metastasis occurs from cancer of the colon in three ways (1) by direct extension to contiguous structures, (2) through hematogenous dissemination to distant sites and (3) by way of the lymphatics to regional or distant lymph nodes

The regional lymph nodes and the liver are the common sites for metastasis of cancer of the colon. Distant and unusual sites of metastatic lesions comprise the lungs, bones, pancreas, renal capsule, spleen, adrenal glands, heart, thyroid gland, breasts, brain, duodenum, and mediastinum

In regard to the nodes involved, there may be retrograde spread and interrupted spread. Normal lymph nodes may intervene between the primary site and the next nearest involved node. In the colloid type of adenocarcinoma nodal metastasis is approximately two and one-half times as great as in the noncolloid type The inguinal lymph nodes are rarely involved in carcinoma of the rectum

Carcinoma of the colon tends to appear in older persons with a little greater frequency than does carcinoma of the rectum. Only 1 of every 20 who have cancer of the rectum and colon will be less than the age of 30 years. Two men for every woman have carcinoma of the colon or rectum

SYMPTOMS The average duration of time which elapses from what is thought to have been the onset of symptoms to hospitalization is around 8 months for those who have cancer of the rectum and 1 year for those who have cancer of the colon. The duration of symptoms before diagnosis is made in patients who have carcinoma of the right side of the colon is about fifteen months

Any symptom sufficient to attract attention to colonic malfunction may be a symptom of a cancer therein Completely asymptomatic cancers of the colon are often discovered by digital, proctoscopic and roentgenologic examinations When symptoms of cancer of the colon are present, they are usually enumerated as altered bowel function, abdominal cramps, pain, and abnormal evacuations of the intestinal contents

The altered function of the colon seems to be a disturbance in the motor functions manifested by constipation, diarrhea, or alternating diarrhea and constipation —much the same sort of disturbance that is present in the irritable colon syndrome. The size, shape and consistency of the evacuated feces, except for the presence of blood, are of no diagnostic import

The situation of the pain and discomfort often does not indicate the existence of the lesion at that site of discomfort The pain may be referred and symptoms may be most prominent in a portion of the colon far removed from the neoplasm. It may [illegible] pain [illegible] ay be [illegible] be referred to the rectum when the lesion is primary in the sigmoid or cecum if there be involvement of the rectal shelf In the presence of obstructing lesions the symptoms are always expressed proximally to the lesion

In carcinoma of the *right side of the colon* there are both general and local symptoms. The symptoms of carcinoma in this region may be illustrated by reference to the predominating symptoms Of 10 patients who have carcinoma of the right side of the colon 6 will have dyspeptic symptoms; 3 will have anemia without

Diagnosis usually is made at the time of surgical exploration. Occasionally the roentgenologist can detect and correctly diagnose this tumor.

Other Benign Tumors. The incidence of other benign tumors of the gastrointestinal tract, and particularly in the colon, is insignificant as compared with the incidence of polyps and lipomas. The other benign tumors are adenomyoma (endometrioma), myoma, fibroma, angioma, lymphoma, neurofibroma, teratoma, enterogenous cysts, cholesteatoma and paraffinoma. These tumors are diagnosed by the same procedures that are employed in polyposis. Often they are discovered accidentally Dermoid cysts may be suspected by noting roentgenologic shadows of teeth or by discovering teeth and hair on proctoscopic examination.

Endometriosis of the Colon and Rectum The etiology, pathology, symptoms and diagnosis of endometriosis are considered in this text in relation to diseases of the female pelvis (see Chapter 7).

It will suffice at this point to summarize the symptoms of endometriosis as follows. The symptoms appear periodically in relation to menstruation and are (1) dysmenorrhea, (2) menorrhagia, (3) sterility, (4) rectal pain or discomfort during bowel movement, increased during menses, (5) diarrhea, worse at, or occurring only during, the menstrual period, (6) bleeding or blood-stained mucus from the rectum or the vagina, appearing with menses, disappearing thereafter, (7) rectal tenesmus and (8) pain on urination or urinary frequency. The common intermenstrual discomforts are (1) *pain in the lower part of the abdomen, pelvis,* and back and (2) dyspareunia

The diagnosis is established by biopsy of endometrial tissue, the history, and the findings on physical examination

Malignant Tumors of the Colon and Rectum. Nine of every 10 malignant tumors of the large bowel represent some variation of *adenocarcinoma* Three of every 100 cancers of the rectum and anus are epitheliomas and practically all are of the squamous *cell type Carcinoids are uncommon tumors of the colon*

Three of every 100 patients who have a malignant lesion will have a *sarcoma* somewhere in the alimentary tract. The majority of intestinal sarcomas are either lymphomatous or fibroblastic in origin

Malignant melanomas are uncommon

Pathology On the basis of their gross appearance adenocarcinomas of the colon may be roughly divided into four main types nodular, scirrhous, colloid, and papillary tumors

Adenocarcinoma of the *nodular* type often is characterized by being a sessile nodular mass which projects into the lumen and tends to encircle the colon Ulceration is common, and if the ulcer is large, the edges are characteristically indurated and nodular This tumor is hard As a result of contraction of the stroma and of inflammation set up in the tissues in and around the tumor by secondary infection in the lesion, distortions and deformities of the colon are common Chronic partial obstruction of the lumen of the rectum or colon is common The colon proximal to the tumor is often dilated or hypertrophied In more advanced obstruction the wall of the colon proximally is thinned and there are present the so-called stercoral ulcers Occasionally perforation occurs with the development of a localized abscess, peritonitis, or a fistula. In the left side of the colon the lesions tend to be smaller and harder than those of the right side

In the *scirrhous* type of adenocarcinoma due to the fibrous element of the tumor, the growth is hard and small, and tends to produce an encircling or napkin-ring type of tumor and colonic obstruction. The scirrhous lesion is found much more frequently *in the left side of the colon than elsewhere It is rare in the rectum*

Adenocarcinoma of the colloid type is uncommon in the colon

Adenocarcinoma of the colon is usually of a relatively low grade of malignancy. The grade of malignancy has been variously classified as follows:

Dukes s classification is based *on the boundaries reached in* either the rectal or the colonic tumors Rectal tumors are divided into three classes. (1) those in which the cancer is restricted to the wall of the rectum (type A, Dukes); (2) those in which

General symptoms, such as loss of weight, weakness, and anorexia, are usually not present until the patient is informed of the possible diagnosis. The tension and anxiety which ensue on knowing the nature of the illness initiate anorexia and subsequent loss of weight.

Carcinoma of the Rectum. SYMPTOMS Those who regularly inspect their stools during health report that there is a change in the character of the stool, an alteration in its regularity, and there may be grossly visible blood on the stool These are confusing symptoms, for they may have been present for years as the result of hemorrhoids, anal deformities, and anal fissures The presence of these symptoms in a middle-aged patient who has never had them previously is significant

Of less importance is a progressive change in bowel habit, because bowel habit yields easily to changes in environment and physical habits As the lesion increases in size, there is a frequent desire to defecate and a disturbing sense of incomplete evacuation, despite a normal defecation, which occasions the use of laxatives, enemas or in some instances paregoric

The pain in rectal carcinoma usually is not severe unless the anal sphincters are implicated or the tumor comes within the grasp of the sphincteric musculature. Extension of the growth into the perirectal structures causes increased severity of the pain The pain may be referred deep in the rectum, to the abdomen, back, hips, and down the thighs

Backache and sciatic distribution of the pain are often present in cancers of the rectum This type of pain may indicate an extension of the cancer along the nerves, and if this is true, surgical removal of the lesion will not relieve this pain

Constipation if present in carcinoma of the rectum becomes more severe than in those who have carcinoma of the colon

The so-called ribbon or pencil stools are of no pathognomonic significance at any time. The final form adopted by the stool is determined mainly by the caliber of the anal canal and the consistency of the feces The caliber of the anal canal which moulds soft feces may be influenced by prolapses of mucosa

EXAMINATION. Patients who have malignant tumors of the colon or rectum usually appear healthy. Some patients who have cancer of the cecum or ascending colon, even though nutrition is good, are pale and sallow Fever is uncommon.

There are usually no abnormal physical findings in the lungs Metastasis to the lungs is ordinarily a late manifestation in cancer of the colon However, when there is early metastasis to the lungs, it is a bilateral disseminated metastasis so that there are no definite physical findings

On palpation of the abdomen a mass is felt in about one third of all cases, irrespective of the situation of the growth in the bowel The mass is often hard, nodular and nontender, and it may or may not be fixed At times tumors of the cecum attain considerable size and the mass may be first discovered by the patient. When there is a lesion of the left side of the colon, in particular, obstruction is likely to be present with audible and at times visible hyperperistalsis, and abdominal distention and tympanites The mass felt in lesions of the left half of the colon is often fecal material proximal to the lesion and not the lesion itself.

Enlargement and hardening of the liver may be present without metastasis When the liver is enlarged from metastasis, often nodules can be felt. In such instances the cancer is advanced, irrespective of the smallness of the primary lesion Ascites may be present as a manifestation of abdominal carcinomatosis. A distorted, hard and fixed umbilicus as a result of metastasis is rare even in widespread abdominal carcinomatosis The inguinal lymph nodes are almost never enlarged as the result of carcinoma in the colon or rectum These nodes are often enlarged in anal, vaginal and scrotal lesions

In examination of the rectum have the patient assume the knee-chest position. The rectum is examined bimanually. A bimanual examination may reveal the pres-

visible loss of blood and with *profound weakness and loss of weight and strength*; 1 will have a palpable tumor However, it is well to know that the clinical symptoms of cancer of the colon cannot be definitely separated, depending on the segment of the colon involved

The patients who have cancer of the right half of the colon often experience a sense of fullness, a tightness, or a feeling as though gas had accumulated and could not move along in the intestine. In some there *may be mild discomfort and abdominal soreness*

The pain, if there should be such, in lesions of the right half of the colon is indefinitely localized to the right side of the periumbilical *region and the right lower* abdominal quadrant and often it is referred to the epigastrium Perforation with abscess formation and extension to the adjoining parietes results in a heightening of the pain and usually a tendency toward its localization.

About one half of the patients who have carcinoma of the right side of the colon have anorexia, bloating, belching, epigastric fullness, nausea but rarely vomiting The anorexia is often the most definite. It is described as an absolute distaste for food. It is the same sort of sensation that is experienced by those who have cancer of the stomach. Subsequent to the anorexia there are weakness in about one fourth and loss of weight in about one half of all patients

Loose bowel motions are common, in lesions of the right half of the colon and some patients have a moderately severe diarrhea. Others have normal bowel movements, or there may be alternating constipation and diarrhea The often described alternation of constipation and diarrhea is frequently associated with the use of laxatives The use of laxatives is probably prompted by the presence of abdominal discomfort A change in bowel habit is a significant symptom which often is self-invoked by medications because of abdominal discomfort.

Like constipation and diarrhea, the presence of mucus and blood in the feces is in itself of meager diagnostic importance Most persons have passed these materials often in their lifetime It is for this reason that the passage of these materials *often* does not frighten the patient The constancy of the presence of blood and mucus in [illegible] be considered as originating [illegible] *from another cause*

In carcinoma of the *left side of the colon* obstruction causes the most definite and often the only symptoms present The presence of rectal bleeding is not a *dependable symptom in lesions in the left half of the colon*

The presence of abdominal pain in lesions in the left half of the colon is variable It may accompany ulceration, perforation or obstruction and becomes more severe as one or all of these processes increase. The pain is poorly localized in the left side of the midabdomen and the lower part of the abdomen A feeling of inability to pass the flatus along may be described The expulsion of flatus often gives immediate relief. Often there is a crampy pain, frequent desire to defecate, and just preceding defecation or while straining at stool there may be a sudden intense lower abdominal pain of short duration In moderately advanced lesions a free expulsion of feces and flatus affords relief. In advanced lesions of the left side of the colon the distress becomes more intense until it is continuous torture

As a symptom of cancer of the left side of the colon constipation is more significant when it appears in one who has never been constipated than in one who has been subject to constipation *Diarrhea may be difficult to evaluate in* a patient who is accustomed to having loose bowel movements Diarrhea is rarely an early symptom of lesions of the left side of the colon

Visible *blood on* the stools is usually due to the accompanying internal hemorrhoids or to chronic anal fissure If bleeding hemorrhoids have been present for a long time, there may have been noticed a little more constancy of the rectal bleeding since the onset of the carcinoma.

the stocky, sthenic somatic type as a result of a wide flaring of rib margins and shallow dome of the diaphragm. Hepatoptosis is found in association with a generalized visceroptosis The right kidney, the stomach and the transverse colon are also displaced downward if there is hepatoptosis

Hepatoptosis exists without producing symptoms

In a great many persons in normal health, when recumbent, the lower border of the liver can often be felt at the right costal edge The position of the upper hepatic border is determined by percussion and can usually be demonstrated at the fifth intercostal space in the midclavicular line With downward displacement of the liver, the lower border can be palpated below its normal site and the upper border is found to have moved down a corresponding distance As the ptosed liver is being palpated, it can usually be rotated somewhat by the examiner's hand, indicating its abnormal mobility. When the liver is low in the abdomen, it may be possible to pass the hand along the upper hepatic surface and between the liver and the costal border. With upward pressure on its lower edge, the liver can often be forced back into a normal position, only to fall from it again when the patient arises.

Situs Inversus Viscerum. The most frequent total displacement of the liver is its transposition seen in association with the transposition of the other viscera in situs inversus viscerum In these cases the liver occupies a position in the left side of the upper part of the abdomen, a mirror image of its normal relationships to the heart, stomach and other organs, since these are similarly transposed. The heart may be transposed without the liver being affected, but transposition of the liver alone is rarely present

Acquired displacements of the liver are seen as a result of diaphragmatic hernia, kyphoscoliosis, and a number of disease conditions of the thoracic and abdominal organs.

The thoracic diseases which may cause *downward displacement* of the liver are effusion or empyema of the right pleura, emphysema, occasionally massive pericardial effusion, and subdiaphragmatic abscess

Upward displacement can result from the pressure of ascites, extreme distention of the bowel, or a large tumor which arises from any of the abdominal or pelvic organs. The liver can be pushed *forward* by retroperitoneal tumors or aneurysm Decrease in size, as in acute atrophy of the liver, permits the liver to fall away from the anterior parietes, and the space it formerly occupied is then taken by intestine

Displacement of the liver does not produce symptoms and frequently is unrecognized

Anomalies of Shape. The primitive or fetal liver is lobulated In an occasional individual the lobulations persist and as a result many lobes have been described. There may be accessory lobes (Riedel's lobe) which, if present, are usually found as finger-like projections from the portal fissure These congenital anomalies have no significance

A *Riedel's lobe* does not cause symptoms Physical examination reveals a rounded, elongated mass appended to the liver and moving with the organ on respiration The mass may extend into the right lower abdominal quadrant It is often tender on pressure There may be some difficulty in deciding, on physical examination, that the mass is a projection of the liver and not a tumor. A Riedel's lobe, if distinctly palpated, is generally found to have a sharp and somewhat firm lower edge

Such conditions as metastatic extensions of malignant lesions, tertiary syphilis, cysts and tumors cause gross structural changes in shape of the liver.

Hepatolenticular Degeneration. There are a number of neurologic syndromes which are associated with a degenerative process in the brain, involving chiefly the lenticular nucleus, and with cirrhosis of the liver.

ence of a lesion too high in the pelvis to be felt digitally. The growth may be a pedunculated polyp or a crateriform ulcer. It is hard unless it is a fungating mass. The size and shape so vary that all forms of descriptive adjectives are applicable. If the tumor is large enough to occupy a great part of the pelvis, digital examination will impart little information as to its actual size, its degree of fixation, and its attachment, if any, to other structures. The tumor may seem to possess all of these undesirable attributes and yet none of these are present It may be fixed in the pelvis *because it is too large to be moved*

In women rectovaginal examination is useful to help demarcate lesions on the anterior rectal wall

Many physicians have not felt a cancer of the rectum since their internship Experience, however, is not necessary to detect a cancer of the rectum. The unexperienced finger can detect the lesion if it be given the opportunity. It is regrettable, though, if a digital examination has not been done when the patient has sought medical advice, for more than half of the cancers of the large bowel occur in that portion which is accessible to digital and proctosigmoidoscopic examination

DIAGNOSIS The diagnosis of malignant lesions of the colon and rectum can be made definitely only after histologic examination of the tissue. Evidence disclosed by digital, endoscopic and roentgenoscopic examinations is all presumptive, but usually proves to be accurate

Carcinomas occurring in those of the younger age group tend to be more malignant than those occurring in older persons. Among women the mortality rate is lower after surgery and survival rates are better than among men The higher the grade of malignancy, the greater the likelihood of metastasis, the higher the operative mortality rate, and the lower the survival rate. In the presence of metastasis to the regional lymph nodes at the time of operation, three fourths of those surviving the operation will eventually die of cancer

The prognosis is better when the lesion is in the right half of the colon than when it is in the left half of the colon, both in patients with, and those without, lymph-node involvement When the lesions are in the transverse colon, because of the ease of infiltration of the stomach and other adjacent organs surgical treatment often is only palliative

THE LIVER

The liver is a large dome-shaped gland situated in the upper right quadrant of the abdomen which is concerned with the production of bile, conversion of most sugars into glycogen which it stores, and the metabolism of proteins and many other substances It has a double blood supply from the hepatic artery and the portal vein

The liver rises to the fourth costal interspace on the right side, to or slightly above the xiphosternal junction in the midline, and to the lower border of the fifth rib on the left side Its extremity, just beyond the apex of the heart, is at the lower border of the sixth rib Its lower border passes from this point to the eighth left cartilage, crosses the middle line about midway between the xiphoid articulation and umbilicus to the ninth right costal cartilage, and thence follows the edge of the ribs posteriorly, being about 1 inch (2.5 cm.) lower in women than in men

The outline of the liver can be approximated by percussion The upper limit of hepatic dullness in the right mammary line extends from the upper border of the sixth rib to the lower edge of the thorax In the right posterior axillary line it reaches the upper border of the eighth, and in the right scapular line, the upper border of the tenth rib. From these limits it extends downward to the edge of the ribs. The lower border can often be palpated in a liver of normal size, depending on the somatic type of the individual.

Anomalies of Position and Shape of the Liver. *Hepatoptosis.* Hepatoptosis is common in tall, thin individuals, though the liver is often palpable in persons of

determinations of fecal urobilinogen are required over a period of time in order to establish the existence of complete obstruction of the common bile duct.

After the intravenous injection of *sulfobromophthalein* (bromosulfalein) the dye is excreted by the liver almost quantitatively A test with this dye is the most satisfactory test for hepatic function in the absence of jaundice. Five milligrams of the dye per kilogram of body weight is the proper dosage. A single specimen of blood is withdrawn by venipuncture at the end of one hour The amount of dye present in the serum is determined by comparison with standardized colors in a colorimeter Retention of dye occurs in about 96 per cent of patients who give evidence of hepatic injury but who have no clinically demonstrable jaundice Occasionally a low-grade retention of the dye occurs without evidence of hepatic disease but this is rare. Marked retention (grade 3 to 4 on the basis of 1 to 4) is the rule with cirrhosis and many other chronic hepatic diseases.

The serum *alkaline phosphatase* may be increased (normal values, adults 1.5 to 4, children 5 to 14 Bodansky units per 100 ml of serum) in obstructive jaundice, while in nonobstructive jaundice the values are often normal or low Limitations are imposed on its use as an indicator of biliary obstruction, since in certain skeletal disorders, and in growing children, increased and varying levels of serum phosphatase are observed

In normal blood serum, *esterified cholesterol* comprises 50 to 70 per cent of the cholesterol In obstructive jaundice there often is an increased concentration of the total serum cholesterol while the cholesterol esters remain normal. In hepatocellular jaundice esterification may be hindered and the concentration of cholesterol esters is decreased In cirrhosis the concentration of cholesterol esters is normal Concentration of cholesterol esters less than 30 mg per 100 ml of serum is indicative of severe hepatic injury.

The sugars *galactose* and *levulose* are nearly quantitatively metabolized by the liver. Galactose is utilized apparently only very slightly if at all by other tissues In obstructive jaundice of long duration without serious injury to the hepatic cells galactose may be metabolized The most reliable information is obtained when the galactose is administered intravenously. The test is useful in the differential diagnosis of obstructive versus intrahepatic jaundice

The levulose test has not gained serious protagonists

The *hippuric acid* test is based on the ability of the liver to conjugate benzoic acid and amino-acetic acid to form hippuric acid This test is time-consuming and certain factors such as renal injury, dehydration and malnutrition affect the final results

Duodenal drainage determines the absence of bile from the duodenum by the color of the duodenal contents If bile is present, liver bile and the darker gallbladder bile (obtained after duodenal instillation of 30 ml of a 40 per cent solution of magnesium sulfate) may be obtained separately

In hepatic disease and in obstructive jaundice before there is serious injury to the hepatic cells, a decrease in supply of *vitamin K* which often is accompanied by a deficiency of blood *prothrombin* is present In the presence of obstructive jaundice there is poor absorption of *vitamin K*, and in hepatocellular jaundice there is a decrease or a suspension of prothrombin production by the liver The administration of vitamin K quickly nullifies any moderate degree of prothrombin deficiency of the blood When there is an absence of prothrombin from the blood because the liver cannot elaborate it, the administration of vitamin K is a worthless procedure

The *cephalin-cholesterol flocculation test* depends on the capacity of the blood serum to flocculate a colloidal suspension of cephalin-cholesterol complex A negative result of the test is one in which no flocculation occurs. The flocculation-inhibiting action of normal blood serum is a function of the albumin fraction of the total protein The test reveals no evidence of the degree of the hepatic injury The cephalin-cholesterol flocculation test is valuable when repeated at frequent intervals so that the trend of hepatocellular jaundice may be determined. Flocculations of grades 3 to 4 (on the basis of 1 to 4) are significant

The mechanisms responsible for the *thymol turbidity test* depend on changes in the serum lipids, the lipoprotein complexes and the gamma globulin fraction of the serum The readings vary from 0 to 4 units Readings of less than 2 are not significant In infectious hepatitis values obtained with this test are not elevated immediately after the onset of the disease Once the values of the test are elevated they remain up during convalescence It does not often give positive results in obstructive jaundice. Consequently

There is a tendency for several siblings to have such diseases, which presumably are definitely heredofamilial. The onset occurs from birth to 9 years of age, but may be deferred to 10 to 19 years of age The course is invariably progressive and often marked by exacerbations. Death usually occurs between the second and fifth years of the disease

There is difficulty in articulation, followed by dysphagia, hoarseness and weakness of the voice and, later, difficulty in mastication Eventually there is a loss of the power of speech and inability to swallow. The face is fixed in a rigid smile, the mouth is open, and saliva drools from it The appearance of the face is identical with that in severe advanced parkinsonian syndrome. Loss of emotional control and exaggeration of emotional reactions are usually present and, in the late stages of the disease, forced laughter and weeping may occur. The skeletal musculature becomes rigid In most cases a cogwheel phenomenon may be elicited, and it is evident that there is an extrapyramidal type of hypertonus A coarse and rhythmic tremor of rest is a constant sign The reflexes are often normal In the late stages of the disease it is impossible for the patients to make themselves understood Death ensues in about 3 years

The cirrhosis of the liver is latent in most instances; however, there may be acute attacks of hepatitis and cirrhosis of the liver.

The *pericorneal pigmentation* is the most important of all diagnostic manifestations. It appears as a narrow zone of greenish gray or greenish yellow overlying the outermost margin of the iris As this zone grows more and more pronounced, it slowly becomes golden The ophthalmologist views this zone with the slit lamp and records that it seems to be composed of fine golden granules lying under Descemet's membrane on the posterior surface of the cornea

The presence of a Kayser-Fleischer ring of pericorneal pigmentation and signs of cirrhosis of the liver are the main positive diagnostic findings. If these features are absent, it scarcely seems to be possible to make the diagnosis

Tests of Hepatic Function (Normal and Abnormal Values) The chief measurable excretory function of the liver is the excretion of bile and thus the bilirubin concentration of the blood Increase in serum *bilirubin* occurs when the production of bilirubin is in excess of the capacity of the liver to excrete it. In hepatitis the hepatic cells and small bile passages are injured so that the bile cannot escape and thus bilirubin accumulates in the blood stream (intrahepatic obstructive jaundice) The commoner cause of increase in serum bilirubin is obstruction of the larger bile passages (obstructive jaundice).

For the determination of the serum bilirubin the quantitative van den Bergh test is preferable to the icterus index. The van den Bergh test measures the total bilirubin present and its reaction (direct or indirect) Normal serums give the indirect reaction, and bilirubin exists in amounts varying from 0.5 to 1 0 mg per 100 ml. In the hemolytic anemias the excess of bilirubin gives an indirect reaction When the serum shows direct-reacting bilirubin, it is good proof of injury to the hepatic cells.

The degree of the increased concentration of the serum bilirubin is of some value in the differentiation of obstructive and nonobstructive jaundice. The greater concentrations of serum bilirubin are observed in acute and severe forms of hepatitis and in malignant obstruction of the common bile duct The intermediate concentrations are observed in milder degrees of hepatogenous jaundice and in the intermittent or partial obstruction of the common bile duct as by a gallstone The lower concentrations are obtained in the serum of a patient convalescing from a subsiding hepatitis or suffering from a portal cirrhosis of the liver

Bile pigment when acted on by bacteria of the colon is converted to *urobilinogen*, and a part of this is oxidized to urobilin which is passed in the feces (normal values of 50 to 300 Ehrlich units). Another part of urobilinogen is absorbed and carried to the liver by the portal circulation and partially re-excreted in the bile. The remainder of the urobilinogen passes into the general circulation and is excreted in the urine.

If the hepatic cells are injured, the part of the urobilinogen excreted in the urine is increased. When the common bile duct is obstructed no urobilinogen appears in the feces Concentrations of from 0 to 10 Ehrlich units in the feces indicate either obstruction of the common bile duct or the suppression of the secretion of bile. Repeated

jaundice as is present in disease of the right side of the heart. Jaundice is a rare complication of heart disease When it does occur as a complication of heart disease it results from hepatocellular injury from chronic passive congestion Congestion alone rarely causes jaundice unless it is of long duration. Hepatic injury due to congestion of long duration often is followed by cirrhosis Cirrhosis of the liver is common in those who have chronic failure of the right side of the heart

In the experience of Walters and Snell, an obstructive jaundice is observed in about two thirds of the patients who have jaundice. However, this group of patients was assembled from a surgical practice In general, in about one half of all instances of obstructive jaundice, the jaundice is due to obstruction of the common bile duct.

Hartman, reviewing records of 400 patients in whom treatment for jaundice was indicated, found that gallstones and associated conditions were the causative factors in about 25 per cent The icterus was due to neoplasms in about 30 per cent of this series, the great majority of such lesions being in the gallbladder, pancreas and bile ducts Benign stricture of the common duct caused the jaundice in 10 per cent of these patients

2. Infectious and toxic jaundice may arise from many and diverse agents or categories of agents which will injure the liver and produce jaundice. Many of these *agents cause an obstructive form of jaundice of the hepatocellular type, while others* produce jaundice of the hemolytic type It is for these reasons that serious objections are made against oversimplified classifications of jaundice like (McNee) the one used here. However, more elaborate classifications of jaundice may prove to be equally confusing

A convenient listing of the commoner categories of infectious and toxic agents which injure the liver and cause jaundice are

(1) The viruses of epidemic hepatitis which includes catarrhal, infectious, endemic, epidemic and possibly homologous serum jaundice, yellow fever, infectious mononucleosis and Rickettsia (a) Secondary bacterial infections in which hepatic injury is not constantly present which may occur in pneumococcic infections (lobar pneumonia) and in miscellaneous infections with organisms such as *Streptococcus pyogenes, Clostridium perfringens* and *Salmonella typhosa* and tubercle bacilli (b) Syphilis (congenital and acquired), and leptospiral infection (Weil's disease) are examples of toxic agents belonging to the Spirochaetaceae and Treponemataceae. (c) Malarial parasites injure the liver (2) The chemical toxins comprise arsenobenzol derivatives, quinoline derivatives, organic compounds and their halogenated derivatives including alcohol, ether, chloroform and carbon tetrachloride, aromatic compounds such as the phenols, benzenes, toluenes, hydrazines and their derivatives, sulfonamides and inorganic compounds, phosphorus, arsenic, lead, gold, bismuth and copper (see Chapter 19) (3) Biologic substances which include mushroom poisoning, snake venom and incompatible blood and hemolytic serums and hemorrhagic disorders of the blood (for example, sickle cell anemia). Many of these infectious conditions and substances are only rarely of clinical importance. They are all discussed in their appropriate places in this text

Cirrhosis increases the susceptibility of the liver to injurious substances

Allergy or increased susceptibility is clearly a cause of development of toxic hepatitis, especially in its relation to the toxic effects of certain drugs It may be the explanation for hepatic reactions to the arsphenamines, sulfonamides, and cinchophen

There is much evidence in recent years which indicates the susceptibility of hepatic cells to injury from dietary deficiencies and malnutrition A potent cause of hepatic disease is often the presence of a chronic generalized affection of the liver. The liver is often affected in disorders of endocrine glands (thyroid diseases), in diseases of the nervous system (lenticular degeneration), in the blood dyscrasias, in diseases of the blood-forming organs and in allergy.

it is most useful in the differential diagnosis of jaundice The thymol turbidity test is positive in a variety of diseases characterized by irritation of the reticuloendothelial cells.

The *serum gamma globulin test* is a turbidimetric test which depends on increases in gamma globulin The reaction appears to be positive in primary hepatic injury and negative in obstructive jaundice

Normal human serum has a total protein content of 6 to 8 gm. per 100 ml About two thirds of this protein is the albumin fraction and the remaining third is composed of the alpha, beta and gamma globulins The total protein content of the serum in patients who have hepatic disease may be normal, increased or decreased. Often the decrease in protein is in the albumin fraction, there may be increase in any of the globulin fractions The concentration of total protein is not altered in obstructive jaundice of short duration It may be decreased in chronic obstructive jaundice. In hepatocellular jaundice low concentrations of total protein are common

Tests of liver functional activity often are of meager diagnostic value in obstructive jaundice *when the obstruction is situated in the extrahepatic bile ducts because* these patients are rarely examined before the hepatitis incident to biliary obstruction has set in There is no measurable difference between the injury to liver cells incident to obstruction of the extrahepatic biliary ducts and that sustained from a primary hepatitis Therefore tests of liver functional activity often fail to be of any very great value in the differential diagnosis between instances of jaundice which can be relieved by surgical treatment

Tests of *liver functional activity are rarely of prognostic value in those who have* jaundice. Like tests for renal functional activity they are of little value unless taken in series with intervals of time elapsing between tests It is the trend of the values given by the succeeding tests which gives the greatest information for both diagnosis and prognosis

Jaundice. THE CLASSIFICATION OF JAUNDICE. Some sort of classification of jaundice is necessary for descriptive purposes Because of its simplicity and wide *applicability McNee's classification is useful and frequently employed* Accordingly, jaundice is divided into three categories (1) obstructive, (2) infectious and toxic and (3) hemolytic (see Chapter 12)

1. In obstructive jaundice the mechanism of the icterus is primarily some interference with the flow of bile This may be due to a lesion such as carcinoma of the pancreas, or to mechanical interference with the extrahepatic bile passages, such as a stone, but it may be a process that causes infiltration of the periportal spaces and thus produces a hindrance to the flow of bile anywhere along its course, beginning within the hepatic lobules In biliary obstruction caused by a carcinoma of the pancreas, for instance, there is within a short period of time injury of the hepatic cells

Obstructive jaundice may be produced by many different intrinsic and extrinsic lesions of the bile ducts. The great variety of these is indicated in the following *enumeration:*

Intrinsic obstructive lesions of bile ducts comprise gallstones, inflammatory exudate, and parasites Intrinsic lesions which may arise in the walls of *the bile ducts* comprise inflammatory changes, strictures, neoplasm, and spasms of the duct or of the sphincter of Oddi

Obstructive jaundice as a part of pulmonary disease may occur as *a complication of pneumonia* (see Catarrhal Jaundice, p 1026). Jaundice often occurs in the presence of extensive *pulmonary infarction due to embolism* or to thrombosis secondary to a *slowed* circulation In instances of slowed circulation, hemolysis is usually the cause of *the jaundice*

[illegible] caused by the pressure [illegible], condition there is injury to hepatic [illegible]

Hepatocellular disease may be manifested as an intrinsic form of obstructive

jaundice as is present in disease of the right side of the heart. Jaundice is a rare complication of heart disease When it does occur as a complication of heart disease it results from hepatocellular injury from chronic passive congestion Congestion alone rarely causes jaundice unless it is of long duration Hepatic injury due to congestion of long duration often is followed by cirrhosis. Cirrhosis of the liver is common in those who have chronic failure of the right side of the heart.

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An excessive protein destruction may occur during prolonged fevers. Inadequacy of glycogen and deficiency of protein both render the liver more susceptible to the action of toxic substances. Likewise a deficiency of vitamins, specifically of the vitamin B fractions, may be important as an etiologic adjunct in the development of hepatic disease.

3. The jaundice in hemolytic icterus is due to an excessive destruction of the erythrocytes. An excessive amount of bilirubin is produced which cannot be excreted by the liver as fast as it is formed. Hemolytic icterus is not a disease of the liver. It is a blood dyscrasia or due to a hemolytic agent circulating in the blood.

Hemolytic icterus may be first brought to the attention of the physician by a patient's reaction to the van den Bergh test There is an increased bilirubin, a (delayed) indirect reaction (see Chapter 12).

In summary it is emphasized that the foregoing classification of jaundice is inadequate The lines of separation of the categories of toxic agents and their exact action on the liver and bile ducts cannot always be drawn The separation of the two groups of obstructive jaundice, namely, (1) the types which arise in the hepatic parenchyma which are not relieved by surgical treatment from (2) the forms of obstructive jaundice due to obstructions of the flow of bile into the intestine and which are relieved, is important

In case of stone in the common duct, in which complete biliary obstruction does not persist for long periods, the degree of distention may not be great, and injury to the hepatic cells may be minimal When malignant disease is responsible for the obstruction it is permanent, until relieved by the surgeon The continued excretion of bile by the hepatic cells further increases pressure within the biliary system, and the smaller canaliculi overdistend and rupture Extravasated pigment enters the lymph and blood spaces of the hepatic lobules, and finally from here passes into the general circulation, thus causing *manifest jaundice*

The degenerative changes which occur in hepatic cells during the course of biliary obstruction tend to disappear when the obstruction is relieved Rarely does mechanical obstruction produce permanent changes in the liver of a sufficient degree to cause cirrhosis However, a form of biliary cirrhosis due to obstruction does occur.

The *absence of bile and of bile salts from the intestines* produces changes in the digestion and absorption of fat. The caloric value of fat is lost The manifestations of loss of the fat-soluble vitamins, A, D and K, may be observed In the adult the loss of vitamins A and D does not produce manifestations of a degree of severity that such a loss may produce in children The loss of vitamin K is an important loss manifested by a prolonged prothrombin time of the blood and hemorrhagic tendencies.

Bile and the components of bile accumulate in the blood The bile stains all of the tissues including the skin and excretions from the body such as the urine and the sweat. The concentrations of the components of the bile, for instance, the cholesterol, phosphatase and bile acids, also are increased The accumulation of these substances in the blood increases the injury of the hepatic parenchyma and destroys the general health

SYMPTOMS. The patient complains of a yellow color which commences in the whites of the eyes and then appears in the skin. As the jaundice develops, nausea, perhaps anorexia and loss of body weight are present. Since jaundice itself is a symptom the attending discomforts are those of the prevailing disease.

The evidence on which it has been concluded that bile salts produce bradycardia and pruritus is incomplete and somewhat faulty. Bradycardia and pruritus are not due to the presence of excessive amounts of bile in the blood, for these are never present in hemolytic jaundice, a condition also attended by excess of bile in the blood

The hepatic cells are adversely affected by the changes which follow biliary

obstruction The degree of hepatic dysfunction as evidenced by tests of hepatic functional activity is somewhat proportionate to the duration and degree of obstruction

As biliary obstruction develops, there are changes in the color of the stool and the urine which in retrospect have been observed by the patient before the discoloration of the skin was evident When gallstones are present, complete obstruction may be transient, so that the character of the bowel movements may be unchanged. With prolonged biliary obstruction the feces are free of bile and are of a light color (putty colored) and remain so for the duration of the obstruction

The urine becomes discolored to deep brownish red in proportion to the amount of bile it contains Intermittent changes in the color of the urine often indicate intermittent obstruction such as that caused by a stone

Examination. The degree of jaundice observed and the size of the liver as revealed by palpation are of relatively little value in regard to the etiology or the diagnosis of obstructive jaundice

The spleen is rarely enlarged early in the course of obstructive jaundice. If the spleen is palpable, the jaundice present is likely to be hemolytic or hepatic in origin.

The essential demonstration to be made by observations and laboratory examinations in obstructive jaundice is the failure of bile to enter the intestinal tract. Absence of bile can be approximately determined by visual examination of the feces The so-called clay-colored stool often indicates the absence of bile In instances in which it is necessary to determine the presence or absence of bile in the intestines this can be accomplished by chemical analysis of the feces for bile (Gmelin's test) or by duodenal intubation Also characteristic of complete biliary obstruction is the disappearance of urobilinogen from the urine and the stool

The most accurate method for measuring the degree of jaundice and observing its course is by repeated determinations of the serum bilirubin concentration by means of the quantitative van den Bergh test An increase in the bilirubin content of the blood begins almost immediately after the onset of obstruction of the common bile duct The speed of the rise and the concentration reached depend on the degree of the obstruction Simultaneous with the rise in serum bilirubin, and often paralleling it, there are usually increases in the total values for blood cholesterol and blood phosphatase.

The most serious blood chemical finding in those who have obstructive jaundice is hypoprothrombinemia, which is an important cause of hemorrhages in this condition Hypoprothrombinemia originates from the absence of bile acids from the intestine and the consequent failure of the intestines to absorb fat and the fat-soluble vitamins, especially vitamin K, needed by the liver to synthesize prothrombin In prolonged biliary obstruction the concentration of prothrombin in the blood decreases sufficiently to permit serious hemorrhages to occur, particularly after surgical operation

The value for prothrombin cannot be determined directly by chemical methods The amount present in the blood can be measured by determining the capacity of the blood to form thrombin and initiate the clotting process.

Quick perfected a one-stage method which utilizes the principle that the coagulation time of blood or plasma is a direct measure of the concentration of prothrombin, provided the other clotting factors, thromboplastin, calcium and fibrinogen, are constant For the purpose of this test, the fibrinogen is considered to be a constant factor, exerting little influence on the rate of coagulation

Consensus is that the simplified one-stage method devised by Quick is satisfactory for the detection of pronounced degrees of hypoprothrombinemia and for the clinical control of vitamin K therapy The normal coagulation time by this method is 17 to 20 seconds

Diagnosis of Jaundice. The differentiation of the obstructive form of jaundice from the hemolytic form is not often a problem Hemolytic icterus is rare, and when

of the congenital variety, it is usually characterized by such distinct clinical and hematologic features as to make its recognition relatively easy. Obstructive jaundice and that due to hepatocellular disease, however, are encountered with about equal frequency The general problem in the diagnosis of jaundice is in reality the differentiation of these two varieties from each other The differentiation is not ordinarily difficult.

In 4 of every 5 cases it is possible to determine at the bedside the type of jaundice from which a patient is suffering. The 1 remaining patient of every 5 may require the utilization of clinical judgment and observations and laboratory procedures over a period of time in order to arrive at a correct diagnosis.

The treatment of obstructive jaundice is fundamentally surgical

Cholemic Nephrosis. Renal insufficiency may result from or be associated with jaundice and hepatic disease. The renal injury that is associated with long-standing obstructive jaundice consists largely of degenerative changes in the epithelium of the renal tubules Whether these changes are produced by the bile substances which the kidneys are forced to excrete or by toxic materials which would normally be destroyed, is not known. The urine is dark in color and heavy with albumin.

Epidemic Hepatitis *(Infectious Jaundice)* The term catarrhal jaundice which formerly was widely used should be employed only when there is cholangitis due to bacterial invasion of the bile ducts such as may occur during the course of infections by the pneumococcus. Terms now preferable to designate the condition formerly called catarrhal jaundice are epidemic jaundice and infective jaundice or infectious jaundice because of the frequent occurrence of the icterus in mild epidemic form. The term epidemic hepatitis is preferable for viral hepatitis or to designate viral jaundice which seems to be the commonest cause of jaundice in patients in the younger age groups

ETIOLOGY Epidemic hepatitis, a disease due to a filtrable virus, has been transmitted to human volunteers The disease is specific for man Attempts to transmit the infection to guinea pigs, white mice, rats, rabbits, hamsters, kittens, gerbils, baboons, chimpanzees, and a variety of monkeys, all have failed

The virus has been found in both the blood and the feces of patients suffering from epidemic hepatitis Epidemics borne by water, milk and food have been described Direct spread by person-to-person contact seems likely, although the experimental evidence indicates that transmission by the intestinal-oral circuit is the most important.

In homologous serum jaundice also of viral origin, the virus is found only in the blood during the incubation period and in the preicteric and icteric phases of the disease

One attack of the infection confers immunity in either epidemic jaundice or homologous serum jaundice and, indeed, these two seem to be the same disease.

PATHOLOGY. The important features in the natural history and pathology of the disease have been described by several observers Lucké described, essentially as follows, his observations based on more than 300 cases in which death occurred, a series of cases, studied through biopsies, in which the disease was not fatal; and a group in which recovery from hepatitis was complete

Biopsies of hepatic tissue reveal that the lesions in nonfatal instances of the disease resemble those of fatal instances in kind but in a milder degree. There are acute necrosis and autolysis of the hepatic cells, and some of the cells contain inclusion bodies which take an acid stain. The damage is quickly repaired, and histologically the lesions cannot be distinguished from those of inoculation hepatitis Furthermore, the changes in sporadic and epidemic cases cannot be distinguished from one another

Postmortem examination of the liver, in cases in which death has occurred from accident or from unrelated disease subsequent to recovery from infectious hepatitis, reveals rapid regeneration.

Residual damage or progressive pathologic change is not observed in cases in which examination is made from 2 months to 3 years after an attack, nor is there evidence of progression to cirrhosis in these cases.

The hepatic lesions may be extensive before the onset of symptoms The degree of

jaundice is not correlated with the severity of the disease. The jaundice is only partly explained by obstruction of biliary canaliculi by bile casts.

The lesions found in cases of hyperacute epidemic hepatitis, namely, those in which the disease is fatal in 2 to 10 days after the clinical onset, have been described by Wood and compared with those in acute homologous serum hepatitis. On the second day the liver cells are already swollen and detached from one another, and by the tenth day they have autolyzed and the debris has been removed Inflammation is most evident in the early stages Wood has emphasized the similarity of the changes to those of acute yellow atrophy. He has expressed the belief that the acute course and high mortality rate in the group (10 per cent) might be explained by the previous poor nutritional state of the patients consequent to war wounds of long standing

Despite the close similarity of the lesions in homologous serum hepatitis and epidemic hepatitis, emphasized by both Lucké and Wood, it appeared from the work of Neefe, Stokes and Gellis that two different agents were involved In their experiments, 6 human volunteers, after recovery from homologous serum jaundice, were immune to reinoculation of the agent, but 5 had jaundice after an inoculation with material containing the agent of infectious hepatitis

Epidemic hepatitis occurs most frequently in persons less than 30 years of age. Occasionally the disease occurs in persons of 50 years or more, particularly during epidemics.

Small epidemics occur in families, institutions, and schools The disease appears most commonly as isolated and sporadic cases

Symptoms A prodromal period of 2 to 7 days is common During this time the symptoms usually present are headache, malaise, anorexia, constipation or diarrhea, nausea and vomiting Mild abdominal pains are frequently present, but in rare instances rather severe pain may occur in the right upper quadrant of the abdomen. Symptoms in the upper part of the respiratory tract are not unusual, and there may also be generalized aches and pain similar to those that occur during an attack of grippe During the prodromal period there may be fever with temperatures ranging as high as 101 F (38 3 C). These symptoms frequently subside in the course of a few days and there may be a relatively symptom-free short period just before icterus is manifested In other instances the symptoms increase in severity at the time that jaundice appears and then slowly subside.

The jaundice begins gradually, if at all, for many who have this disease are never jaundiced, although in an occasional patient the icterus may seem to come on acutely, sometimes developing overnight. The onset of icterus is frequently forecast by a darkening of the color of the urine followed by an icteric tint of the scleras and face Once it begins, jaundice usually increases rapidly in intensity The time of occurrence of a maximal degree of icterus and the duration and severity of the discoloration also vary widely The duration of the jaundice is usually measured in days; in an occasional instance this may extend into weeks or, rarely, months.

Symptoms alleged to be associated with icterus, such as bradycardia and pruritus, occur with variable frequency in epidemic hepatitis and are no more important than the amount of discomfort they give the patient

Examination. During the course of epidemic hepatitis the liver often increases appreciably in size, its edge usually being somewhat rounded and slightly tender In protracted disease the liver may seem firm With improvement, there is a gradual decrease in hepatic size Very rapid decrease in the size of the liver, as measured by percussion of the upper and lower borders, is an ominous sign, particularly if the patient becomes more icteric and more prostrated In such a case the development of acute yellow atrophy is suspected Splenic enlargement of moderate degree is observed in from one third to one half of the patients. Since this ocurs only rarely in obstructive jaundice, discovery that the spleen is enlarged is a sign of diagnostic importance

The number of blood cells may be within the normal range, or there may be mild leukopenia with relative lymphocytosis.

Determination of the serum bilirubin concentration furnishes the only accurate method for measuring the intensity of the icterus. The appearance of the urine, however, does afford a simple method of following the course of the disease, since a decrease in the discoloration of the urine is frequently one of the first signs of improvement. Only rarely are stools completely acholic during the course of an attack of epidemic hepatitis, although the amount of bile pigment they contain is commonly reduced. In those instances in which the stools have been acholic, a reappearance of bile-stained stools is a sign of improvement The significant laboratory findings in epidemic hepatitis are those revealed by the various liver function tests It does not matter which of the many that may be employed are used. The proviso is that they must be correctly interpreted If the tests are performed early in the course of the disease, within the first two weeks in the average case, definite evidence of hepatic cell disturbance is usually noted The galactose tolerance test has been particularly valuable for this purpose and the reaction has been positive in about 80 per cent of cases of epidemic hepatitis if the test is performed during the acute stages. Other tests, such as the hippuric acid test and the cephalin-cholesterol flocculation, thymol turbidity, zinc sulfate tests, and others also usually give positive results in the early phases of epidemic hepatitis

DIAGNOSIS A patient who is young and who gives a history of the onset of jaundice after prodromal gastrointestinal symptoms or symptoms simulating grippe, without a history of contact with hepatotoxic drugs, usually has epidemic hepatitis The liver and the spleen are often enlarged Diagnostic tests of liver function usually give evidence of hepatic cell dysfunction. The subsequent rapid improvement that commonly follows the acute onset is also rather characteristic and aids in confirming the diagnosis

Differential diagnosis requires primarily the exclusion of the possibility of jaundice due to mechanical biliary obstruction This type of jaundice is rare in persons of the age of the average patient who has epidemic hepatitis but must be considered in those who are in or beyond middle life The two most important types of obstructive icterus are those due to cholelithiasis and those due to carcinoma of the head of the pancreas Differentiation of these two types of obstructive jaundice from catarrhal icterus is usually fairly easy clinically. When difficulties are encountered, these often arise from failure of the gallstones to cause pain, the occurrence of pancreatic malignant disease in a young patient and the development of epidemic hepatitis in one who is older than the usual patient who has this type of jaundice. Those who have the disease without jaundice may not be detected unless severe liver injury is sustained.

PROGNOSIS. Lucké quoted mortality rates of various epidemics of hepatitis, particularly those occurring among military personnel These range from 0.13 to 0 44 per cent. He was able to examine the livers of 14 patients who had recovered from attacks of epidemic jaundice Lucké concluded that complete restoration of the hepatic parenchyma occurs in nonfatal hepatitis and considered this a natural consequence of the acute and noncontinuous injury to the hepatic cells.

The prognosis of epidemic hepatitis is good, as stated Occasionally, however, there is a transition from what at the onset seemed to be an ordinary example of the usually mild disease to a process of great severity which may end fatally. Termination of epidemic hepatitis in acute hepatic atrophy is further evidence of the underlying injury to hepatic cells that is present in some cases. Yellow atrophy develops only rarely, because the causative factors are not ordinarily severe enough to over-
[illegible]r.

[illegible] mologous serum hepatitis
[illegible]ns of measles convalescent

serum had been given This observation was followed by reports of jaundice which developed subsequent to the administration of vaccines containing human serum The disease was widely studied when it appeared among military personnel who had received yellow fever vaccine containing human serum as a diluent.

Homologous serum hepatitis is a viral disease.

The very nature of viral hepatitis *precludes the possibility of determining* whether the disease has been transmitted by blood or its derivatives and thus called homologous serum hepatitis, or whether it is due to acute infectious hepatitis.

It is noteworthy that about 26 per cent of the patients studied by Ratnoff and Mirick received injections of arsenicals or other medicaments and did not receive blood or a derivative This substantiates the observation that the virus may be transmitted from a known patient or a carrier by skin puncture with an improperly sterilized instrument Instruments contaminated with virus require heat sterilization by autoclave or by boiling in water for 15 minutes Hence, when viral hepatitis appears after transfusion of blood or its products, it is difficult to establish whether blood or another avenue of infection is responsible

Because whole blood is used more frequently than plasma, whole blood transfusion is responsible for more cases of homologous serum hepatitis than plasma transfusion From 11 to 12 per cent of patients cited by Ratnoff and Mirick had received only blood, 2 to 3 per cent received both plasma and blood, 2 patients received plasma alone; 1 patient received icterogenic yellow fever vaccine, and 1 patient received human globulin Other investigators report a 0 2 to 0 4 per cent incidence of hepatitis following whole blood transfusion The percentage incidence is higher with plasma than with whole blood because transfused plasma is usually derived from a pool of many samples; one infected sample, by contaminating a whole pool, endangers all recipients. One report presented an incidence of 3 4 per cent possible and 2 1 per cent probable hepatitis following transfusion with unsterilized plasma Another report recorded an incidence of *5 per cent*

Ultraviolet irradiation will inactivate the virus of hepatitis in icterogenic serum A method of sterilization of serum and plasma has been approved as satisfactory by The National Institutes of Health However, it has been shown that this method can fail when large quantities of plasma are being processed

The symptoms are similar to those of infectious hepatitis, but in general they are somewhat less severe.

The findings on examination are identical with those of epidemic hepatitis

The history of having received human blood or products of human blood from 60 to 180 days prior to onset of the illness is diagnostic

Recovery is expected Improvement begins 1 to 2 weeks after the jaundice reaches its peak Early mortality rate is about 0 2 per cent. Massive necrosis with rapid hepatic insufficiency may suddenly occur during convalescence The cirrhosis which may follow epidemic hepatitis is either a nodular cirrhosis (Mallory) or rarely a biliary cirrhosis

Toxic Jaundice. The toxic substances themselves may cause direct injury to the hepatic cells or may act as a form of allergy or hypersusceptibility. Chemicals such as hydrazine derivatives, toluenediamine, arsine and hemolytic serums may injure the liver from the hemolysis produced in the blood (see Diseases due to Chemical Agents, Chapter 19) Direct injury to the hepatic cells is the mechanism of action of such substances as phosphorus, various dyes, and fat-dissolving chemicals such as carbon tetrachloride, chloroform and others of the halogenated hydrocarbons. The mechanism by which arsenicals and sulfonamides inflict injury on the liver is unknown (see Chapter 19)

Arsenical Hepatitis. The hepatitis which may follow the arsenical therapy of syphilis was formerly among the most important hepatocellular injuries of chemical origin. That the jaundice is produced by some direct action of the drug on the liver seems most likely.

In arsenical hepatitis there are degenerative changes of the parenchyma which vary from cloudy swelling and edema to actual necrosis. This may be focal or diffuse and, if of a sufficient degree, may warrant a diagnosis of acute yellow atrophy. In some cases pericholangitis and the deposition of bile thrombi in the smaller bile passages occur, producing an intrahepatic form of obstructive jaundice which can be clinically recognized by the absence of evidences of hepatic dysfunction ordinarily considered characteristic of degeneration of hepatic cells.

SYMPTOMS. Jaundice may follow very small dosage of the arsenical drugs administered by mouth or intravenously. After the first dose or after only a few doses the toxic effects on the liver are manifested by jaundice.

Two forms of jaundice follow treatment with arsenicals, an early and a late form The early type may follow within 1 to 15 days after an injection. The late variety may not appear until 4 or 5 months after the last arsenical treatment has been given.

Icterus may occur alone or may be preceded by fever, chill, general malaise, nausea and vomiting and, in some instances, pain in the right upper abdominal quadrant In the delayed type of paratherapeutic jaundice toxic symptoms are less frequent than in the early variety. In both forms the icterus reaches its peak in about a week Then there may or may not be prostration and malaise. Itching is occasionally severe. Pronounced loss of body weight may ensue

The icterus persists for variable periods. The majority of patients recover completely within 4 to 6 weeks. Systemic manifestations usually subside long before the jaundice disappears, although pronounced asthenia may remain for long periods.

EXAMINATION. There is hepatic enlargement in more than one half of the cases Splenic enlargement may be present in 1 of every 10 cases. Ascites may develop during the course of the icterus and gradually disappear as recovery takes place

There are no characteristic blood findings which would aid in the diagnosis of postarsphenamine jaundice

In the majority of cases of paratherapeutic icterus the tests of hepatic function indicate the presence of acute injury of the hepatic cells

DIAGNOSIS. If arsenicals have been administered and there is found no other cause for the icterus, it is assumed that arsenic is the etiologic agent. Arsenical therapy can be considered the possible cause of icterus occurring as long as 6 months after therapy has been given

The majority of patients who have arsenical hepatitis make a complete clinical recovery in a few weeks Acute yellow atrophy may ensue in a few instances

Jaundice Following the Use of Sulfonamides. Jaundice which follows the administration of one of the drugs of the sulfonamide group may be produced as a result of an acute hemolytic crisis and profound anemia, or may be due to direct toxic injury to the liver and the development of hepatitis or both.

The basis for the development of hepatic dysfunction and clinical hepatitis subsequent to the use of sulfonamides is not clear The presence of antecedent disease of the liver is not often responsible In some instances specific drug hypersensitivity seems to have been the responsible factor

The pathologic changes induced in the liver by sulfonamides are primarily degenerative processes The characteristic feature is an extensive focal necrosis In some instances this has been sufficiently extensive to cause changes resembling those of acute yellow atrophy.

The amount of sulfonamide which will cause hepatitis varies considerably. Hepatitis may follow one dose or many doses.

Unlike the icterus which follows the acute hemolytic anemia caused by sulfonamides, jaundice due to hepatitis does not occur early in the course of the chemotherapy. Icterus may not ensue until several days or weeks have passed after the discontinuance of administration of the sulfonamide

SYMPTOMS. The onset of the jaundice is usually insidious and not preceded by other symptoms. However, chills and fever and systemic symptoms of varying

severity may occ... gradually increases for a week or 10 ... ic enlargement is generally ...

Tests of hepatic function usually reveal evidence of dysfunction of the liver.

DIAGNOSIS. The onset of jaundice while one of the sulfonamide drugs is being administered, or shortly thereafter, is the chief clue to the nature of its origin. The presence of definite hepatic dysfunction and the absence of anemia or of evidence of hemolysis serve to exclude the possibility of acute hemolytic anemia.

The prognosis of sulfonamide hepatitis varies considerably with the severity of the poison In general the prognosis is favorable. It is unwise to administer sulfonamides to patients who recover from the hepatitis.

Cinchophen Hepatitis. In recent years the use of cinchophen has decreased sharply, with a corresponding reduction in the number of cases of toxic hepatitis which it produced

The toxic effects of cinchophen have been classified by Parsons and Harding as follows (1) *cutaneous manifestations* such as pruritus, angioneurotic edema, urticaria, and macular and papular rashes, (2) *anaphylactoid reactions* characterized by neurocirculatory disturbances; (3) *gastrointestinal disturbances,* including ulcers of the mouth, heartburn, nausea, vomiting and diarrhea; and (4) *hepatic involvement* as indicated by the appearance of jaundice, which varies in degree and may range from transitory icterus to acute yellow atrophy.

Beaver and Robertson described the lesion of cinchophen hepatitis as acute atrophy with profuse acute parenchymatous degeneration and necrosis

Anorexia, nausea and vomiting, and pruritus may precede the jaundice. However, the jaundice commonly begins insidiously, and is usually painless, with or without fever. The icterus reaches its maximum in the course of a few days. In those killed by cinchophen, the icterus gradually increases in intensity until death occurs. In the nonfatal instances the jaundice lasts for a variable length of time; in some for more than 2 months There may be hemorrhage from esophageal varices When the condition is fatal, progressive stupor, coma and delirium may be expected. The terminal rise in temperature so characteristic of "liver death" is frequent

On examination an ascites may be present The size of the liver varies considerably The liver may be enlarged in those patients who are not seriously ill The spleen is often enlarged in the prolonged illnesses

Diagnosis depends on knowledge that the patient is taking the drug or has had it The clinical features of cinchophen hepatitis are indistinguishable from those produced by other forms of toxic or infectious injury to the liver

A poor prognosis is indicated by persistence and increasing intensity of the jaundice, the development of mental symptoms, the appearance of hemorrhagic phenomena, oliguria, hyperazotemia and increasing hepatic dysfunction as indicated by results of liver function tests One half of those who have cinchophen jaundice die.

Acute Yellow Atrophy of the Liver. Numerous terms, including acute necrosis and subacute necrosis of the liver, have been used to designate the disease states characterized by destruction of the hepatic cells

Acute yellow atrophy of the liver is characterized by jaundice, decrease in the size of the liver, hemorrhages, and nervous symptoms which usually terminate in coma and death It is a rare disease of early adult life.

The consensus is that all of the various noxious agents such as drugs, metabolic poisons, and infections which under certain conditions produce only a mild hepatitis, might, on occasion, induce the severe changes which terminate in acute yellow atrophy.

In an editorial in the Journal of the American Medical Association it was pointed out that the incidence curve of acute yellow atrophy of the liver has presented three peaks during the last three decades. The first period of excessive frequency was from 1918 to approximately 1924, inclusive, that is, the years immediately following World

War I. The second peak occurred from 1928 to 1934, inclusive, and the third abnormal increase in such cases was recorded during World War II and immediately after. A different etiologic factor has been advanced for each of these three epidemic-like appearances of acute yellow atrophy An accentuated toxic effect of arsphenamines on the liver because of a lowered resistance of this organ resulting from prolonged insufficient nutrition was blamed for the first wave of acute yellow atrophy, mainly recorded from Germany and Austria; starvation had been prevalent there during the last years of World War I and the years thereafter. The second increase in reports on acute yellow atrophy coincided with publications on the specific hepatotoxic action of cinchophen preparations, these had been used to an increasing degree since 1912 for the control of various painful conditions The last peak was related to the occurrence of virus-conditioned infectious hepatitis among the combatants of the various nations fighting in the Mediterranean theater of war, although smaller local epidemics were recorded from other parts of Europe and America during this period.

A critical analysis of the evidence on which the etiologic claims as to the hepatotoxic role of arsenicals and cinchophen were based throws serious doubts, according to the editorial, on the validity of these explanations. Postarsphenamine jaundice, postcinchophen jaundice and infectious jaundice are clinically, biochemically and pathologically indistinguishable from one another In regard to the hepatotoxic action of arsphenamines it was noted at that time that an appreciable number of patients with acute yellow atrophy who were observed after World War I had not received injections of these drugs

Snapper reported that arsphenamine treatment given to the generally undernourished North Chinese did not elicit at any time an increased incidence of acute yellow atrophy, refuting thereby the claim that the combination of lowered hepatic resistance through starvation and a chemotoxic action of arsenicals on the liver was responsible for the temporary numerical rise in the incidence of acute yellow atrophy during the years following World War I A direct, nonallergic hepatotoxic action of arsphenamines in these cases is improbable, since the amounts of these drugs normally used in the treatment of syphilis are definitely below a hepatotoxic level Recent observations on the transfer of infectious hepatitis, which may lead to acute yellow atrophy, have shown that improperly sterilized needles and syringes may play an important part in this respect The introduction of infected homologous serum may occur not only with the injection of human plasma, but also accidentally, during routine venipuncture with syringe and needle for blood samples for blood sugar determinations or similar tests, or during routine intravenous injections of arsphenamine, pentothal sodium, penicillin and other drugs The observations reported in this respect by Marshall are particularly instructive, according to the American Medical Association editorial He observed in 50 per cent of the patients receiving arsenicals intravenously the development of jaundice on about the hundredth day after the first injection, when special precautions were not applied to the sterilization of the needles and syringes There was no case of jaundice after a special new syringe for individual use was boiled before and after injection Inasmuch as infectious hepatitis was observed among the soldiers participating in World War I, the distinct likelihood exists that the transitory increase of acute yellow atrophy in the postwar period was essentially not of arsenotoxic origin but of infectious nature.

There exists now little definite evidence favoring the concept that the second wave of cases of acute hepatitis resulted from a hepatotoxic action of cinchophen. Apparently cinchophen and its derivatives do not exert a direct, nonallergic hepatotoxic effect in various species even when given in lethal doses or in toxic doses over a long period There were for some years cinchophen preparations on the market which were given intravenously Yellow atrophy was not seen among the patients of several institutions in which cinchophen preparations were administered routinely and over a considerable number of years; several physicians each observed more than 1 case of yellow atrophy despite a restricted use of the drugs in their private practice. There is also no plausible explanation for the fact that the hepatic complications allegedly caused by cinchophen made their first appearance some 15 years after the introduction of the drug and that few cases of cinchophen hepatitis have been reported during the last 8 years despite a considerable continued use of cinchophen during this time in this and other countries

During the last 20 years similar claims concerning the cause of acute yellow atrophy

of the liver have been made for a number of other therapeutic chemicals. The evidence presented suggests that the existence of an infectious hepatitis represents for at least some of them a distinct possibility and should be kept in mind for future occurrences of this type

PATHOLOGY. On gross examination the liver is diminished in size, in some cases to even less than half the normal The color is yellow or yellow streaked with red The liver is soft and is easily torn

When the liver is cut, its softness is even more apparent. The cut surface is often of the same yellow or mingled red and yellow color as that of the intact surface. Involvement is not uniform and the disease process may vary considerably in different portions of the liver.

The spleen is usually enlarged Degenerative changes may be present in the pancreas, and profuse hemorrhages occur throughout the gastrointestinal tract. The renal lesions consist of granular and fatty degeneration in the convoluted portions of the tubules. The glomeruli are normal.

SYMPTOMS The symptoms before the appearance of jaundice consist of anorexia, nausea, vague abdominal discomfort, vomiting and diarrhea There is a low fever, weakness, headaches and generalized aches and pains

The jaundice of acute yellow atrophy commences insidiously about 2 weeks after the onset of the preicteric symptoms With the developing jaundice there is an increase in the gastrointestinal disturbances Malaise, anorexia and prostration become totally incapacitating Often there is pain in the hepatic region There soon are severe headaches, photophobia, and restlessness, and a tendency to delirium and convulsions ensues Urinary and fecal incontinence often appear. As the acute hepatic atrophy advances, there is vomiting of blood and bleeding from the bowel. There may be vaginal bleeding or hemorrhages from the mouth and nose and into the skin If acute hepatic atrophy occurs in a pregnant woman, abortion ensues and there is profuse vaginal hemorrhage

As death approaches, there is a subsidence of the delirium and restlessness, and the drowsiness and stupor increase until final coma supervenes. Associated with the coma is a progressive rise in temperature until death

The duration of the entire course of the disease is variable Death usually occurs in from 3 to 5 weeks after the beginning of the icteric stage of the disease

EXAMINATION The characteristic observation on physical examination from time to time is the progressive decrease in the size of the liver In the more severe instances of the disease the shrinking may be so great that the hepatic percussion dullness completely disappears Ascites may be demonstrated in some patients, particularly in those who survive for longer than the average period of time (6 or more weeks) Associated with the ascites there may be edema of the lower extremities

There is a moderate decrease in the erythrocytes The concentration of bilirubin in the serum increases to as much as 30 or 40 mg per 100 ml The qualitative van den Bergh reaction is of the direct type The value for fasting blood sugar is often low The total blood cholesterol is low The cholesterol esters and urea may disappear from the blood The prothrombin time is increased, owing to the combined influences of faulty absorption of fat-soluble vitamin K from the bowel and inadequate synthesis of prothrombin by the liver False positive serologic reaction (Wassermann) may be obtained The urine is bile stained, usually contains albumin, and may show numerous casts

DIAGNOSIS The symptoms of the preicteric stage followed by intense jaundice, nervous and mental disturbances, hemorrhages, and laboratory evidence of changes in metabolic function of the liver are diagnostic In patients who have abdominal pain with the jaundice, the onset of coma indicates that the disturbance arises from more severe causes than those which produce simple mechanical jaundice

Acute yellow atrophy of the liver is generally a fatal disease. In this disease the

outcome is more predictable from the seriousness of the symptoms than by any other means

Pyogenic Abscess of the Liver. Hepatic abscesses are rare but they may occur in association with systemic pyogenic infections, in certain parasitic diseases, and in trauma, and finally there are the primary idiopathic hepatic abscesses. In the idiopathic abscesses it is impossible to demonstrate an antecedent causal focal infection or to isolate an infective organism.

Pyogenic abscess or abscesses of the liver occur oftener in young adults than in members of other age groups and affect the sexes equally.

Hepatic abscesses are commonly caused by *Escherichia coli*, the streptococcus, the staphylococcus, and varying combinations of these organisms. Anaerobic nonhemolytic streptococci have rarely been cultured from abscesses of the liver.

Hepatic abscesses in association with staphylococcal septicemia are the commonest of all In *Staphylococcus aureus* infections a latent period usually supervenes between the focal staphylococcal infection and the development of hepatic abscesses. This latent period may be of several months' duration after a carbuncle due to the *Staphylococcus aureus* has seemingly healed Very often the pus in pyogenic abscess of the liver is sterile as well as the cultures. Abscesses of the liver occur more frequently after appendical infections than in any other disease

Abscesses of the liver are single in one half of the cases Multiple abscesses occur from infections reaching the liver through pylephlebitic or hepato-arterial routes Single abscess occurs several times more frequently in the right than in the left lobe and is usually found near the dome of the liver In instances in which an abscess has been present from 1 to 2 years, granulomatous changes are often marked

Chills, fevers and sweats are common symptoms. Fever, usually of the remittent or intermittent type, is the first symptom present; the temperature ranges between 100 and 104 F (37.8 and 40 C).

The daily occurrence of chills is common in association with hepatic abscesses There is dull pain over the liver In some the pain may be situated in the axillary line, in others the pain may extend to the lateral lumbar region Anorexia, loss of weight, and weakness, dyspnea and a hacking, nonproductive cough may be present

On examination slight guarding of the rectus muscle in the upper right quadrant of the abdomen often is present. Limitation of expansion of the right lower portion of the thorax with dullness and rales at the base of the right lung is common Pleural effusion on the right side and empyema may be present in cases of single pyogenic abscess of the liver. Elevation of the diaphragm together with restriction in mobility is commonly found

In single pyogenic abscess of the liver, jaundice is not common, but in association with multiple abscesses of pylephlebitic origin it frequently is present The presence of jaundice in any case of liver abscess implies a grave prognosis.

Laboratory procedures reveal albuminuria in the presence of high fever Bile may appear in the urine when there is jaundice. Leukocytosis is commonly present. The more chronically and seriously ill patients have anemia

The procedure of aspirating pus from the abscess and injecting thorium dioxide into the abscess cavity to delineate its size, shape and position is not recommended

In those who have fever and chills and have pain and tenderness in the hepatic region with enlargement of the liver and an elevated diaphragm on roentgenologic

: abscess and amebic abscess of
be a *history of dysentery*, often
chronic and recurring. The demonstration of *Endamoeba histolytica* from the stools strongly favors the diagnosis of amebic abscess.

All of
ing

hepatic abscess The roentgenologic findings may serve to distinguish these two lesions

The prognosis of hepatic abscess is almost invariably hopeless unless surgical operation is performed Pleural and pulmonary complications adjacent to the diaphragm and subphrenic abscess are likewise conditions for surgical treatment. Operations are not advised in the presence of pyemia and abscesses in the lungs, kidneys, spleen or brain

Syphilis of the Liver. Syphilis of the liver is of either the congenital or the acquired type, depending on the mode of infection and the age at which the infection begins.

Congenital Hepatic Syphilis. In congenital syphilis the liver is increased in size and the hepatic changes tend to be diffuse. The surface is smooth The color of the liver is lighter and possesses a gray, grayish yellow, or yellowish tinge On section the organ may be firmer than is normal The cut surface may show small gray spots due to syphilomas or miliary gummas The spleen is enlarged and is much firmer than the spleen of a healthy infant Amyloid disease occurs in some of the older children.

Many children who are born alive and survive for a few weeks appear healthy The abdomen is usually prominent owing to enlargement of the liver and spleen and to tympanites

The physical findings of congenital syphilis include the cutaneous, mucosal and bony lesions together with anemia, and wasting or enlargement of the liver and spleen In some the enlarged liver may be palpated in the region of the iliac crest Ascites is common The spleen is enlarged in about half of the cases Jaundice is often present, and may be of the intermittent type Congenital hemolytic icterus has been recorded in association with congenital syphilis of the liver

The diagnosis is not difficult in the presence of the foregoing physical findings. A positive serologic reaction will be present in either the mother or the child

Delayed Congenital Syphilis of the Liver. Ten to 20 years is the average age of patients afflicted with late congenital hepatic syphilis These patients are poorly developed and often exhibit signs of infantilism The syphilitic lesions involve the liver, the sense organs and bones Amyloid disease is often present Hepatic enlargement, splenic enlargement and ascites are commonly found and may be associated with jaundice.

The foregoing findings in association with Hutchinson's teeth, deafness, interstitial keratitis, or infantilism are diagnostic. Without these findings the diagnosis of acquired syphilis is more safely made than when they are present If a tumor is palpated, the possibility of hepatic cysts or malignant disease of the liver is entertained If ascites is a prominent finding, tuberculous peritonitis, Banti's syndrome and hepatic cirrhosis are possible diagnoses

The prognosis in late congenital hepatic syphilis is grave

Hepatic Lesions During the Secondary Stage of Syphilis. The occurrence of jaundice during the secondary stage of syphilis is rare If an arsenical drug has been administered, the differentiation between syphilitic jaundice and arsenical jaundice will be impossible

A presumptive diagnosis may be made if there are the history of a recent chancre and the presence of the syphilitic exanthem At this stage of the disease the serologic reaction is usually positive, but not invariably so

Hepatic Lesions During the Tertiary Stage of Syphilis. The tertiary lesion of hepatic syphilis is the gumma, which is often associated with fibrotic changes, the result of healing O'Leary has estimated the incidence of hepatic syphilis among patients admitted to the Mayo Clinic for surgical or medical treatment, or both, as

[illegible] of hepatic syphilis in cases of tertiary
[illegible] clinical means and, in most instances,

Tuberculosis of the Liver. Hepatic tuberculosis has little clinical significance The liver commonly is involved, along with other organs of the body, in the terminal stages of miliary tuberculosis, but local tuberculosis confined to the liver is exceedingly rare.

Actinomycosis of the Liver. Hepatic actinomycosis is extremely rare. Abdominal distention, abdominal pain and tenderness, and the palpation of a mass often constitute the preliminary clinical manifestations Later the liver is enlarged and often tender, and fever is frequently present. Jaundice and ascites seldom occur but anemia and varying degrees of leukocytosis are common. The diagnosis depends on the recovery of the ray fungus from the discharging abscess of the liver, abdominal wall, pleural cavity, or other region

Diseases of the Liver Due to Infection by Higher Animal Parasites. Clonorchiasis. All known species of the superfamily Opisthorchioidea belong to the family Opisthorchiidae The species parasitic in man are *Clonorchis sinensis, Opisthorchis felineus, Opisthorchis viverrini* and *Opisthorchis noverca*

The fluke *Clonorchis sinensis*, causative agent of clonorchiasis, is a parasite of fish-eating mammals in Japan, China, Formosa, Korea and French Indo-China Man and other mammals become infected by eating raw or imperfectly cooked fish

The changes produced by *Clonorchis sinensis* are localized in the distal biliary passages, particularly of the left lobe of the liver. The injury to the host depends on the number of worms, a few parasites causing little damage, but large numbers producing serious and progressive hepatic disease The irritative action of the parasite and its toxic secretions produce an adenomatous proliferation of the biliary epithelium with thickening of the walls of the ducts and formation of crypts

Early light infections are without appreciable symptoms The characteristic early symptoms [illegible]
liver wit [illegible]
heavier [illegible]
infections these symptoms are aggravated by the involvement of the hepatic circulation, and ascites and cachexia.

The diagnosis is based on finding the characteristic ova in the feces Patients seldom die from clonorchiasis

Opisthorchiasis. *Opisthorchis felineus* is found in man only in the highly endemic areas of East Prussia and Poland, in the Ob Basin of Siberia, and in the Philippines and India.

The hepatic lesions produced by *Opisthorchis felineus* are similar to those caused by *Clonorchis sinensis*

The symptomatology in general resembles that caused by *Clonorchis sinensis.* There may be fever, chills and sweating, loss of appetite, abdominal pain, frequent yellowish watery stools, enlarged liver, slight jaundice, a polymorphonuclear leukocytosis and anemia

The diagnosis is made by finding the characteristic ova in the feces.

Fascioliasis (*Liver Rot*). The flukes are parasitic worms of the class Trematoda of the phylum Platyhelminthes

All members of the superfamily Fascioloidea belong to the family Fasciolidae. One species, *Fasciolopsis buski*, is an important intestinal parasite of man Two other species, *Fasciola hepatica* and *Fasciola gigantica*, are accidental parasites of man. *Fasciola hepatica* is the cause of liver rot

The habitat of the fluke is the biliary passages

Although the endemic center for liver rot is Cuba, the geographic distribution is cosmopolitan where sheep husbandry is practiced. In the United States of America the disease occurs along practically all the coastal streams where the pasture ground is low and thus a natural habitat for suitable species of snails

In heavy infections the migrating larvae may produce extensive destruction of the liver in animals. The pathologic processes result from the mechanical, irritative and

toxic actions of the parasites Hepatic enlargement is followed by portal cirrhosis with atrophy of the hepatic cells and portal vessels.

The symptoms are those of acute hepatic and biliary disease. There are pain on pressure over the liver, jaundice, irregular fever and persistent diarrhea. The patient may be profoundly toxemic with cachexia and anemia from the effects of hepatic damage and perhaps from the absorption of the toxic products of the living and dead worms The ingestion of raw infected liver may be followed by symptoms of suffocation resulting from the pharyngeal attachment of adult worms

Diagnosis is established by finding the ova in the feces or in material obtained by biliary drainage. The presence of ova in the feces of persons who have recently eaten infected liver may not be indicative of infection, since the ova pass undamaged through the intestinal tract

The prognosis is grave in heavy infections

Dicrocoeliasis. The species of fluke, *Dicrocoelium dendriticum*, infecting man belongs to the family Dicrocoeliidae This fluke is common in Europe and is found in northern Africa, Asia (Syria, Turkestan, Siberia and China), and in North and South America

The principal definitive host is the sheep. The intermediate hosts are the snails.

The adult worms inhabit the biliary tract. The immature worms first invade the biliary capillaries and later descend to the main ducts and gallbladder.

There may be vague digestive disturbances, for instance flatulence, chronic constipation, diarrhea and enlargement of the liver.

The diagnosis is made by finding the characteristic ova consistently present in the feces Their temporary presence may result from the ingestion of poorly cooked infected liver.

Perihepatitis. Perihepatitis exists in both acute and chronic forms

Acute Perihepatitis. Penetrating wounds and intrahepatic disease which reaches the surface of the liver result in perihepatitis Perihepatitis may have its origin in the thorax and may reach the tissues surrounding the liver by a spread through the diaphragm.

An active local congestion of the upper surface of the liver is followed by the formation of a plastic exudate which, during healing, may become absorbed or may form adhesions to adjacent structures

A constant symptom of acute perihepatitis is pain in the region of the liver which may extend to the epigastrium or to the shoulder and which is made worse by deep breathing or movements of the body The presence of a dry cough, hiccough and shoulder-tip pain is indicative of diaphragmatic irritation

On examination there may be observed limitation of motion of the right side of the thorax and guarding of the abdominal muscles in the right side of the hypochondrium. The liver may be tender In some instances a friction rub synchronous with respiration can be heard over the liver

In the presence of intra-abdominal or intrahepatic infection the occurrence of sharp pain in the hepatic region is suggestive of perihepatitis. The diagnosis of acute perihepatitis, except the gonorrheal form in women, is not made clinically.

Acute Gonococcal Perihepatitis. A woman who has a proved gonorrheal salpingitis may have an acute gonorrheal perihepatitis months or even years after having had an acute salpingitis Acute gonorrheal perihepatitis is said to be characterized by adhesions between the anterior surface of the liver and the abdominal wall

There may be a history of antecedent lower abdominal discomfort, menstrual irregularities, fever, leukorrhea, and dysuria. There is a period of quiescence of pelvic symptoms from the gonorrhea or there may have never been any pelvic symptoms from gonorrhea before the sudden onset of pain in the region of the liver. The pain is severe, beginning in the right upper abdominal quadrant, and passing through to

the scapular region or to the right shoulder tip. Nausea, vomiting, upper abdominal distention, headache, sweats, and chilly sensations and fever accompany the acute pain. The temperature rises from 99 to 103 F (37.2 to 39.4 C) with a corresponding acceleration of the pulse rate. Rapid shallow respirations may be present.

On physical examination abdominal distention may be pronounced. The liver is palpable Muscle guarding and tenderness of the abdominal wall in the right upper abdominal quadrant are constantly present. Physical signs of poor aeration of the lower lobe of the right lung are commonly obtained A transient to-and-fro friction rub may be present during the early stages of the disease. Pelvic examination, however, usually reveals evidences of active or passive inflammatory changes in the uterine tubes.

Examination of the blood reveals a moderate leukocytosis accompanied by an increase in the nonfilamented neutrophils A rapid sedimentation rate of the erythrocytes is the rule and it may persist long after the acute process has subsided. Gonococci are usually identified in the urethral and cervical smears or cultures, although failure to demonstrate the organisms does not render the diagnosis untenable. Fitz-Hugh reported the recovery of gonococci from peritoneal exudate in 1 case during the subsiding stage of the disease

Diagnosis. Positive cultures on special mediums for growth of the gonococci from vaginal smears or aspirated pus are diagnostic The evidence of pelvic inflammation followed by the forementioned symptoms and physical findings is sufficient for a presumptive diagnosis unless there are reasons which render the diagnosis untenable

The outlook is uniformly good

Chronic Perihepatitis (*Polyserositis*) Chronic inflammation of the capsule of the liver, either localized or generalized, is termed chronic perihepatitis This rare disease has also been variously designated chronic peritonitis with perihepatitis, chronic hyperplastic perihepatitis, multiple serositis, polyserositis, simple diffuse chronic peritonitis, chronic obliterative peritonitis and chronic exudative peritonitis

The etiologic agent is unknown. The disease occurs in both men and women of middle life

Chronic perihepatitis is characterized by the formation on the surface of the liver and the gallbladder of a thick layer of fibrous tissue There is often an extension from an acute inflammation, particularly the localized form. Adhesions are commonly present between the liver and contiguous structures The spleen is enlarged The omentum becomes shortened and thickened so as to produce a palpable mass in the abdomen The right pleura is more often thickened than the left. The pericardium is less frequently affected than the pleura

There are transient attacks of pain in the right upper abdominal quadrant. Progressive ascites which requires repeated paracentesis is the rule. However, a chronic ascites may accumulate and remain for years without causing a constitutional symptom or requiring paracentesis. In some, chronic renal insufficiency develops and then edema ensues. The disease may progress until all of the serous cavities are filled with fluid and there is a general anasarca

The diagnosis can be made only at operation or at necropsy. Eventually death occurs as a result of intercurrent infection or circulatory failure

Cirrhosis of the Liver. Cirrhosis of the liver is often a degeneration or an atrophy of the parenchymal cells with hypertrophy of the interstitial tissues Often it seems that inflammation progresses simultaneously with destruction of the hepatic

[illegible] gnosed,

namely, (1) portal, (2) toxic and (3) biliary.

Portal cirrhosis is the ordinary form of the disease. Laennec's cirrhosis or alcoholic cirrhosis is included in the diagnosis of portal cirrhosis In advanced portal cirrhosis there is an obstruction to the portal circulation. It is the consensus that a portal cir-

rhosis includes the end stages of toxic, infectious, nutritional, or circulatory disturbances of the liver.

It is accepted that *toxic cirrhosis* is the late result of necrotizing lesions of the liver. In toxic cirrhosis there is death of the hepatic cells and collapse and condensation of the stroma so that the liver is irregular in shape and small in size. It is almost characteristic of toxic cirrhosis not to cause symptoms, and the disease is recognized only at necropsy

Biliary cirrhosis arises from biliary obstruction The site of the inflammatory processes is around the bile ducts The severity of the lesion depends on the degree and duration of the obstruction, and the presence or the absence of infection.

Portal Cirrhosis. (*Laennec's Cirrhosis, Atrophic Cirrhosis, Alcoholic Cirrhosis, Hobnail Liver*) This is the common form of cirrhosis which frequently affects middle-aged men

In recent years data have accumulated which indicate that in cirrhosis of the liver there are disturbances of fat and carbohydrate metabolism and deficiencies of protein and certain vitamins The known importance of alcohol in the development of cirrhosis in certain patients is just beginning to be delineated by its relationship to vitamin (vitamin B) deficiencies.

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Repeated injury to the hepatic cells or failure in recovery from acute injury from infection or toxic agents because of unfavorable nutritional factors may result in degenerative changes in the liver and in the development of all of the pathologic and clinical features of cirrhosis

The incidence of alcoholism among cirrhotic patients is high Some persons who consume quantities of alcohol do not eat enough good food. Over long periods they eat at very irregular intervals and in insufficient amounts, and subsequently they enjoy gross dietary overindulgences It may be that alcohol plays an important part in the development of cirrhosis of the liver because the diet of those who drink heavily often is inadequate and cirrhosis follows as a consequence of dietary deficiency, or because alcohol may induce certain metabolic disturbances of the hepatic cells which lead to excessive deposition of fat which, in turn, may cause cirrhosis. Fleming and Snell expressed the opinion that portal cirrhosis was alcoholic in origin in 42 5 per cent of their 200 cases

Bollman and Mann produced a lesion similar to that of portal cirrhosis by repeated administration of sublethal doses of carbon tetrachloride or of tetrachlorethane. Substances such as these, and the heavy metals, arsenic, lead and mercury, however, are only rarely important in the production of human cirrhosis (see Chapter 19).

Metabolic and Endocrine Disturbances The incidence of cirrhosis in *diabetes* is low, it was reported by Wilder to be only 0.7 per cent in 2,584 cases

Injury to the liver is common in *hyperthyroidism* Beaver and Pemberton found that these hepatic injuries range from acute degenerative lesions to subacute toxic atrophy and toxic cirrhosis Thyrotoxicosis is responsible for relatively few instances of cirrhosis, but it may be important as a causative factor in an individual case.

In human beings fatty livers develop in the course of starvation, diabetes and alcoholism Cirrhosis may result from certain specific deficiencies also which either favor deposition of fat in the liver or deprive the hepatic cells of elements needed for their internal metabolism These deficiencies seem to have a constant relationship to vitamin B deficiencies

Prolonged and severe congestion of the liver is a factor in the production of the hepatic disturbances Chronic passive congestion of the liver often occurs in association with congestive heart failure In these cardiac patients there are ascites, jaundice and splenomegaly.

THE CIRRHOTIC PROCESS The cirrhotic process produces alterations in the vascular relationships within the lobule Destruction of the parenchyma and contraction of the fibrous tissue bring the central veins closer to the portal spaces.

The studies by McIndoe of corrosion specimens of cirrhotic livers showed that there is great diminution of the total vascular bed The main portal trunks are attenuated and stenosed and the smaller portal vessels are distorted and twisted. There is an almost total loss of normal relationship between the portal and the hepatic arterial circulations In perfusion experiments McIndoe was able to show that from 86 to 100 per cent of fluid introduced into the portal vein passed into collateral channels rather than into the hepatic vein. The hepatic tissue had become almost entirely dependent on the hepatic artery for nutrition.

The forcing of the portal blood into other channels is responsible for the development of collateral circulation and often results in hemorrhage, for example, from esophageal varices The body is deprived of the metabolic and detoxifying functions of the liver since blood from the gastrointestinal tract is shunted into the general circulation without coming in contact with the hepatic cells. The regenerative ability of the liver is markedly reduced when portal blood is prevented from reaching the organ

The capsule of the liver is thickened, and the surface is uneven and studded with nodules, uniform in size and distribution. The variations in size of the nodules and the contraction of the fibrous tissues between them cause the liver to be extremely irregular in contour

Cirrhosis is essentially a disease of late middle life. The disease occurs at a somewhat earlier age in women than in men. It may occur in children The higher incidence of alcoholism in men is ordinarily given as the explanation for a higher occurrence of cirrhosis among them than among women

Environmental rather than constitutional factors determine the differences in race incidence The disease occurs in all races under comparable environments

SYMPTOMS. Snell reviewed the early symptoms in 112 cases in which ascites had already developed He listed the early symptoms as anorexia, flatulent indigestion, jaundice, abdominal pain, asthenia, diarrhea, hematemesis, vomiting, edema, enlarged liver or spleen, and pruritus Ascites had developed suddenly and without warning in 18 per cent of these cases

Anorexia may be profound and lead to marked loss in weight The digestive disturbances may result from the effect of cirrhosis on the secretory and absorptive functions of the gastrointestinal tract Flatulent indigestion consisting of belching of sour material is commonly associated with anorexia.

Abdominal pain occurs in 1 of every 3 cases of portal cirrhosis It is usually localized to the right upper quadrant or to the epigastrium but may be generalized No obvious explanation can be found The pain may be associated with jaundice, weakness and diarrhea.

Hemorrhagic phenomena, such as epistaxis, occur with fair frequency in cirrhosis. These may be the result of hypoprothrombinemia in some instances and thrombocytopenia in others It is more probable, however, that localized vascular disturbances are the principal cause of the hemorrhages Grave hematemesis may be associated with esophageal varices.

Cerebral disturbances, comprising the loss of concentrating ability, confusion, restlessness, depression, delirium and actual psychoses, may occur

Fever occurs in cirrhosis in the absence of inflammatory processes After persisting for a long period, the fever may disappear spontaneously only to recur later in the course of the disease

EXAMINATION. On examination may be found a type of vascular cutaneous change, the *spider nevus*, that is characterized by a central point from which radiate fine branches for a distance of about 1 cm. Patek found that these nevi either consist of an artery and its arteriolar branches or resemble an arteriovenous anastomosis (glomus). Nevi occur over the sternum, the upper part of the thorax, the *shoulders*, and occasionally on the lower part of the trunk and on the legs.

Often there is a superficial vascular change in the palms of the *hands (palmar erythema)* (see Hands, Chapter 6). This palmar erythema is manifested by flushing

of the thenar and hypothenar eminences and is observed in active cirrhosis and in nutritional deficiency, regional enteritis and chronic ulcerative colitis. It seems to be associated with decreased concentrations of serum albumin.

Pruritus is fairly common in cirrhosis, and may be independent of the occurrence of jaundice

Collateral Circulation The locations for collateral circulation in portal obstruction in the gastrointestinal tract are (1) at the cardiac end of the stomach and at the anus, (2) at the site of an obliterated embryologic circulation, through the falciform ligament and para-umbilical veins and, rarely, through remnants of the umbilical vein The collateral circulation through these channels is responsible for the formation of the distended veins which may often be found on the abdominal wall of a patient who has cirrhosis. Collateral circulation occurs (3) at situations where the gastrointestinal tract, or its glands or appendages, becomes adherent to the abdominal wall, developmentally or pathologically

In the course of physical examination it may be observed in some that the collateral circulation between the portal system and the superior and inferior caval systems has produced visible distention of these veins on the anterior abdominal wall and, in rare instances, may result in the formation of the caput medusae (cirsomphalos), a cluster of dilated veins around the umbilicus with the direction of blood flow away from the umbilicus

Distended veins which connect the portal system with either the superior or the inferior vena cava usually occupy the midportions of the abdominal wall, and this situation of the veins serves somewhat to distinguish them from the collateral circulation which forms when the caval system is obstructed In obstruction to the portal circulation the blood distending the veins flows upward in the veins of the upper one third of the abdomen and downward in the veins of the lower two thirds.

Slight icterus is present in one half of those who have cirrhosis. The jaundice may appear at any time in the course of cirrhosis, but it is rarely prominent in the early findings It is common for a hyperbilirubinemia to persist once it has begun

The liver is often enlarged, and it remains about the same size during the entire period of observation

It may be difficult to palpate the spleen in an abdomen distended by fluid or gas Splenic enlargement is commonly found late in the disease in association with ascites It may be found early in the course of cirrhosis and may be present for a long period before other definite evidence of the disease appears The spleen may fluctuate in size considerably and decrease after a hemorrhage

Ascites is present in more than one half of those who have a cirrhosis of the liver Edema of the lower extremities is present in 1 of every 3 who have an advanced cirrhosis of the liver The reason for the edema is the hypoalbuminemia caused by the cirrhosis Hydrothorax may be present and it may be unilateral or bilateral

Peripheral neuritis, paraplegia, absence of deep reflexes, hyperalgesia of the muscles and nerve trunks of the legs, and drop foot may be present in those who have cirrhosis of the liver and chronic alcoholism

Anemia is observed commonly in patients who have cirrhosis The anemia is a natural consequence and is due to malnutrition, bleeding and hepatic injury

The anemia of cirrhosis is often of the macrocytic variety and moderate in degree The erythrocytes are uniform in size with little or no anisocytosis or poikilocytosis

The leukocyte count varies considerably in the course of cirrhosis. Leukopenia is fairly common

The concentration of serum bilirubin is increased in a great many cases of cirrhosis, not only in those in which clinical jaundice is present but also in many in which there is no indication of jaundice. The degree of bilirubinemia is ordinarily not excessive.

There is a decrease in the excretion of sulfobromophthalein, when employed as a test of liver function, in a patient who has cirrhosis of the liver.

A decrease in the concentration of serum albumin is commonly observed in cirrhotic patients, particularly if ascites is present. The decrease in concentration of serum albumin is probably a specific result of hepatic dysfunction. Many patients who have an advanced cirrhosis have increased concentration of the serum globulin, with inversion of the albumin-globulin ratio.

The urine is usually decreased in amount and of a high specific gravity. It contains increased amounts of urobilinogen and may contain bilirubin if the patient has jaundice

Biopsy in Cirrhosis of the Liver. The correlation between clinical and laboratory observation and the histologic features as revealed by bits of liver obtained for biopsy indicate that the evidence of diffuse damage to hepatic cells is more closely identified with objective clinical and laboratory observations than with coagulation necrosis, infiltration with fat, focal necrosis or leukocytic reactions. This suggests that injury to hepatic cells is the most important factor in determining the clinical activity in cirrhosis Hepatic tests performed within 2 to 7 days of the biopsy reveal that the cephalin flocculation and thymol turbidity tests appear best to indicate the presence of diffuse injury to hepatic cells in cirrhosis In the presence of cell injury in cirrhosis there is a serum-albumin reduction and to a lesser degree a serum-globulin elevation and reduction of albumin-globulin ratio Patients who have an alcoholic history reveal, in general, less damage to hepatic cells and more infiltration with fat than those without such a history Ascites coincides most with scarring and other phenomena associated with fibroplasia and inflammation in the portal triads and in the connective tissue trabeculae. The type of cirrhosis associated with jaundice does not reveal specific morphologic characteristics except for the presence of static bile pigment.

Contraindications to Needle Biopsy of the Liver Attempts to needle a small liver are dangerous because of the ease with which a loop of bowel can be perforated Kleitsch and Kehne never do needle biopsies if the edge of the liver cannot be definitely palpated. A prolongation of the clotting or bleeding time should contraindicate this procedure. In some cases it may be possible to lessen the bleeding time of the patient by the administration of vitamin K, but should the hemorrhagic diathesis persist, biopsy should not be attempted Another important contraindication is obstructive jaundice, the reason being that dilatation of the peripheral biliary radicles will make perforation of one of them by the aspirating needle likely When one of these dilated biliary radicles is perforated, there is a tendency to establishment of a biliary fistula which, in turn, will produce a bile peritonitis The authors described such an experience which followed needle biopsy of a patient in whom jaundice was due to carcinoma of the head of the pancreas.

DIAGNOSIS The diagnosis of cirrhosis of the liver in its early stages is difficult and uncertain Liver biops
less or causes symptoms
disturbance The presence
man who has grade 2 (c
when administered as a test of liver function, is sufficient for a diagnosis This test is inaccurate in the presence of jaundice When jaundice exists, some such procedure as the thymol turbidity test should be employed The combined information given by the sulfobromophthalein, urobilinogen, hippuric acid and cephalin-cholesterol flocculation tests and the determination of the serum-albumin content is much greater than that given by any one of these tests alone

The diagnosis of fully manifested cirrhosis when there are ascites, hematemesis, persistent low-grade jaundice, splenomegaly, and visible collateral venous channels is not difficult.

the disease is usually fairly rapid

In portal cirrhosis acute [illegible] pneumonia, erysipelas, and non-

tuberculous peritonitis, are frequent. Tuberculosis is frequently a terminal event Hernias are relatively common in patients who have cirrhosis, particularly in those who have ascites

Of patients who die directly of cirrhosis, approximately one third die of hemorrhage and two thirds die of progressive failure of the liver The terminal event is often called cholemia, of which coma is the characteristic feature.

Toxic Cirrhosis. (*Postnecrotic Cirrhosis, Nodular Cirrhosis*). A toxic cirrhosis follows many forms of poisoning by drugs or chemicals and sometimes acute infectious hepatitis and occasionally in a patient who recovers from acute or subacute yellow atrophy In this form of cirrhosis ascites occurs late in the course of the disease if at all.

Cirrhosis of the Liver in Children. Cirrhosis in children is rare Among 82,866 admissions to the St Louis Children's Hospital there was a total of 40 cases of cirrhosis

Defined as a diffuse fibrosis of the liver, the condition can be brought about in a variety of ways, some of which depend on inheritance and some on major derangement in some other organic system A variety of toxins are capable of causing necrosis in the liver which, if it is not too extensive, is followed by fibrotic repair There seems to be nothing distinctive about this sequence as it occurs in children Two typical cases of hepatolenticular degeneration, which have been described, are indistinguishable, so far as the liver is concerned, from ordinary nodular cirrhosis

Keller and Nute classified the disease, according to causes, in the 40 cited cases There were 8 cases of obstructive biliary cirrhosis, which is due almost always to congenital anatomic anomaly Clinically it is distinguished by an obstructive jaundice in the newborn infant and pathologically by interlobular fibrosis, bile stasis and moderate inflammatory infiltration Eleven patients had nodular cirrhosis, which develops in childhood rather than in infancy and is insidious in onset Jaundice and hepatosplenomegaly are the most constant observations The atrophic stage is rare The liver shows extensive perilobular fibrosis, focal regeneration and mononuclear cell infiltration without bile stasis Diffuse fibrosis of the liver, in addition to the usual clinical and pathologic findings, was observed as a rare sequela of erythroblastosis fetalis in 5 cases Congestive cirrhosis is the result of repeated severe passive congestion of the liver that alternates with periods of relative compensation Clinically it is overshadowed by the primary disease of the heart Six cases of this type are reported There was only 1 case of postnecrotic cirrhosis of the liver.

The manifestations of cirrhosis of the liver in children are similar to those present in adults who have a comparable form of the disease

Biliary Cirrhosis. (*Hanot's Cirrhosis, Cholangiolitic Cirrhosis, Noncalculous Cholangitic Cirrhosis*) Biliary cirrhosis occurs in a primary and a secondary form. The *primary* form occurs in youth and early adult life It may be familial It is characterized by persistent jaundice and enlargement of the spleen and the liver, fever, leukocytosis and mild abdominal pain

The *secondary* form of the disease seems to be a sequel of a persistent obstruction of the common bile duct This disease is suspected if jaundice does not subside after the obstruction of the common bile duct has been relieved

Vascular Diseases of the Liver. Cirrhosis of the liver due to chronic passive congestion has already been considered Hemangioma likewise has been mentioned Other vascular diseases of the liver are rare and are seldom diagnosed prior to death

The portal vein may become occluded and in rare instances a complete collateral circulation ensues When the portal vein is occluded and collateral circulation is not adequate or not established, there is sudden onset of hematemesis, ascites and swelling of the spleen

The hepatic veins are subject to occlusions, periphlebitis, suppurative phlebitis and endophlebitis A widespread occlusion of the hepatic veins which results in an excessive collateral circulation about the umbilicus is known as Chiari's disease

(endophlebitis hepatica obliterans). Diseases of the hepatic veins are even rar than disease of the portal vein.

The hepatic artery may be involved by atherosclerosis, by infarcts or by aneurysm. All of these conditions are rare and usually are not diagnosed clinicall

Tumors of the Liver. *Benign Tumors.* Benign tumors of the liver are ra lesions which occur more frequently in men of middle age than in men of oth ages or in women. These growths may be either solid or cystic. The solid tumo include angioma (hemangioma and lymphangioma), adenoma (fibro-adenoma benign teratoma (mixed tumor), hamartoma, leiomyoma, lipoma and teratoma

Hemangioma, the most frequent benign tumor of the liver, occurs in the left lob These tumors are usually single, demarcated and often pedunculated, but they var through wide limits in size and locations in the liver

Adenomas arise either from liver cells or bile-duct cells and may be single c multiple. They too vary in size and location

Teratomas are solitary tumors of variable size and consistency.

Growths composed of all the cellular elements of the hepatic parenchyma have bee given the name *hamartomas* The mass is composed of liver lobules, bile ducts an blood vessel networks which, though fairly well differentiated, may not show any pur poseful arrangement or attain the complete pattern of the normal organ. Hamartoma which occur in the lungs are not composed of hepatic tissue but of a network of newl formed blood vessels

Leiomyomas in the liver are exceedingly rare lesions.

The symptoms of benign solid tumor of the liver arise when the mass reaches size sufficient to interfere with the normal function of neighboring organs Thus th symptoms produced are variable The most definite symptoms arise when there i sufficient pressure on the common bile duct or the intestine to occlude the lumer of the structure involved

On examination there is a palpable, nontender, smooth mass connected with the liver The mass, most commonly, is palpable in the midepigastrium Hemangioma may present as a palpable mass in the left upper quadrant Some hemangiomas may be compressible, and occasionally a bruit or hum may be heard over them An enlarged spleen, ascites, and other evidences of portal hypertension and decompensation may be observed when the tumor, especially an adenoma, is associated with cirrhosis of the liver

Benign solid tumor of the liver is diagnosed on biopsy of a specimen removed by the surgeon or at postmortem examination The diagnosis may be conjectured if there is a mass associated with the liver or directly connected with the liver, and if the mass has been known to exist for a long time without any serious deterioration in the health of the patient

Surgical removal when possible, is the only treatment.

There are *parasitic and nonparasitic cysts* of the liver As a matter of enumeration the following cysts may be identified solitary (simple, retention), multiple (in polycystic disease), echinococcal (hydatid), cystadenoma, pseudocyst, teratomatous, lymphatic (lymphangiomatous), and endothelial These cysts are identifiable only by biopsy

The echinococcal cyst is the only important *parasitic cyst* affecting the liver, and the resulting disorder is the only important acquired cystic disease of that organ (see Infection of the Intestines by Higher Animal Parasites, p 939).

Hepatic nonparasitic cysts, solitary or multiple, are rare.

Solitary cysts have been observed in fetuses and in persons of all ages Nonparasitic cysts remain symptomless unless they attain sufficient size to compress adjacent viscera, or unless complications develop Medical advice is sought because of painless abdominal swelling Abdominal pain, when present, is epigastric or is situated in the right upper quadrant.

Rupture and infection are frequent complications in nonparasitic cysts. In addi-

tion, sudden intracystic hemorrhage may occur with an accompanying acute abdominal pain. Much the same manifestations are seen in the rare case in which the pedicle of a large pedunculated cyst suddenly becomes twisted

Physical examination reveals an abdominal tumor In polycystic disease both kidneys are nearly always palpable as well as the enlarged liver.

When some complication occurs in cystic disease of the liver, the findings depend on the complication present

A correct diagnosis is not made prior to operation or death. Sinuses may persist for years when treatment by external drainage has been employed.

Malignant Tumors (Primary). The clinical features of malignant tumors of the liver are the same for all types

Among the factors thought to be of importance in the genesis of primary cancer of the liver are previous or existing inflammatory processes, parasitic infection, chemicals, dietary deficiencies, congenital defects, hereditary predisposition, trauma and venous congestion An evaluation of the importance of these factors, singly or combined, is not possible

Cirrhosis of the liver is associated with primary carcinoma of the liver in 8 of 10 who have malignant hepatomas and in half of those who have malignant cholangiomas. Thrombosis of the portal vein is common in primary carcinoma of the liver. Thrombosis of the hepatic veins occurs occasionally, and even thrombosis of the inferior vena cava may be present

Pathologists describe sarcomas, malignant teratomas and carcinomas. The primary carcinomas of the liver are divided into three groups (1) the hepatocellular carcinomas (hepatomas), (2) carcinomas of the gallbladder or bile passages (cholangiomas) and (3) the atypical or mixed carcinomas Hepatomas are the most frequent form of primary cancer of the liver All of the carcinomas of the liver are often associated with cirrhosis

In sarcomas of the liver, the liver is usually much enlarged and the lesions may be massive, nodular, or conglomerate and diffuse Cirrhosis, as in carcinomas, is frequently associated if the sarcoma arises primarily in the liver

Intrahepatic metastasis is so common as to be almost the rule in fatal primary malignant tumor Extrahepatic metastasis occurs in one half of all cases The sites most frequently affected in extrahepatic metastasis are the regional lymph nodes and the lungs

Primary hepatic carcinoma may occur in persons of any age, including children. It is commoner in the pigmented races than in the white race

SYMPTOMS In children the attention of the parents is often initially attracted by a large abdomen or the appearance of an abdominal mass In others loss of weight, vomiting, nutritional disturbance, anorexia, or abnormal stools arouse concern Jaundice and ascites are not nearly so common in children as in adults

In adults there commonly are, in retrospect, loss of strength and progressive loss of weight which are more rapid than should be attributed to the cirrhosis of the liver, which is responsible for the ascites, peripheral edema, collateral venous development and hematemesis In others the symptoms are those of malignant disease which is responsible for the loss of weight, asthenia, pain and hepatic enlargement without the features of cirrhosis

Three out of 4 patients who have primary hepatic malignant disease have abdominal pain which is localized to the right upper abdominal quadrant and not infrequently is felt in the back as well It is unrelated to meals, and rarely is severe until the disease is well advanced Asthenia, as a rule, is delayed in appearance until the disease is well advanced

Hematemesis or melena, or both, from ruptured esophageal varices, and epistaxis, frequently recurrent, are common. Occasionally pruritus is intense and constitutes one of the important complaints. Hypoglycemic episodes with hunger, diplopia, nervousness and even coma may occur

Fever is not a feature of the disease and rarely is present

(endophlebitis hepatica obliterans). Diseases of the hepatic veins are even rarer than disease of the portal vein.

The hepatic artery may be involved by atherosclerosis, by infarcts or by an aneurysm. All of these conditions are rare and usually are not diagnosed clinically

Tumors of the Liver. *Benign Tumors.* Benign tumors of the liver are rare lesions which occur more frequently in men of middle age than in men of other ages or in women These growths may be either solid or cystic The solid tumors include angioma (hemangioma and lymphangioma), adenoma (fibro-adenoma), benign teratoma (mixed tumor), hamartoma, leiomyoma, lipoma and teratoma

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Rupture and infection are frequent complications in nonparasitic cysts In addi-

Hourglass gallbladders are common. Irrespective of whether they are of congenital or acquired origin, they are symptomless However, a gallbladder containing an hourglass deformity may become diseased.

A *diverticulum* of the *neck* of the gallbladder is usually a persistent fetal cysthepatic duct or rest. Diverticula found in the *fundus* may be due to a constricting band of fetal origin. A diverticulum of the gallbladder responds in unison with the gallbladder to disease and stone formation.

A gallbladder having within it small partitions which communicate with each other is a *trabecular gallbladder.* Such an organ originates from a vesicular outgrowth of hepatic tissue.

The *malpositions* of the gallbladder in the horizontal plane comprise transposition of the vesicle to the left when it is situated on the undersurface of the left lobe of the liver, and situs inversus viscerum in which the gallbladder is moved to the left side as a part of the general malformation. The malpositions in horizontal transverse planes comprise deep embedment of the vesicle in the liver and retrodisplacement, in which the gallbladder does not rest in its own fossa, and the fundus extends back and adheres to the liver or hangs free and retroperitoneally.

The gallbladder is normally intrahepatic during early developmental stages, but it becomes *extrahepatic* during development. When intrahepatic in man, the vesicle usually is found partially or completely embedded. Diagnosis is made at surgical operation or at necropsy

Acquired anomalies of the gallbladder may resemble true diverticula. For instance, there may be eventrations of the wall of the gallbladder and cul-de-sacs which are multiple and contain calculi. Hydrops and displacements due to disease of the liver or adjacent structures are commonly observed.

Acute Cholecystitis. Acute inflammation of the gallbladder is commonest among stocky, stoic, obese persons. More women are affected than men Negroes are infrequently affected.

Acute cholecystitis most frequently arises from an obstruction to the outlet of the gallbladder by an impacted gallstone in the proximal end of the gallbladder or in the cystic duct. Rarely are obstructions present such as torsion of the cystic duct at its junction with the gallbladder, or obstruction of the cystic duct by congenital narrowing or by an anomalous blood vessel More commonly, when acute cholecystitis occurs in the absence of gallstones, it is from obstruction of the cystic duct from acquired fibrosis or from extrinsic compression from enlarged lymph nodes or from an adjacent tumor.

There are many gallbladders which remain bacteriologically sterile throughout the course of acute cholecystitis Occasionally, acute cholecystitis is due to bacterial infection, but such occurrences are rare and then they may be associated with stagnant bile in the gallbladder

The gallbladder in acute cholecystitis of moderate degree is enlarged The peritoneal surface is covered with an inflammatory exudate, and there may be adhesions to surrounding structures In the more severe infections gangrene may be present with some exudation of bile-stained fluid to the outside of the gallbladder. In some instances the fundus of the gallbladder may be embedded in the hepatic parenchyma and is surrounded by a localized necrosis Occasionally there is a free perforation of the gallbladder with an associated generalized chemical peritonitis If the gallbladder has become adherent to the duodenum or colon, free perforation into the bowel may be present.

Symptoms. The symptoms may commence at any time, during the day or night with pain in the epigastric or in the right hypochondriac regions. There may be nausea and vomiting of varying degrees of severity from the beginning of the attack or these symptoms may be postponed until after the patient has had an opiate administered for the pain The vomiting often is retching and almost continuous.

When first seen by the physician, 7 or 8 of every 10 patients will mention that they have had similar attacks before. In the severe attacks pain is constant, sharp and severe However, variations in intensity of pain occur during an attack. The pain in acute cholecystitis usually returns after the effect of an injected opiate wears

EXAMINATION. In both children and adults enlargement of the liver is rapid and tremendous The liver may be fixed and may not display mobility either on palpation or with respiration In those who have cirrhosis of the liver prior to onset of carcinoma of the liver, the spleen is palpable and ascites is present. Edema of the legs may ensue Jaundice is present late in the course of the disease.

Studies of the blood reveal anemia Liver function tests, analyses of the feces and the urine, and roentgenologic examination do not reveal any worthy diagnostic data.

DIAGNOSIS. A very rapid enlargement of the liver in the absence of failure of the right side of the heart and without any other evidence of hepatic disease may be due to a primary tumor Diagnosis of primary malignant neoplasm of the liver is seldom made prior to necropsy or biopsy.

Primary malignant neoplasm cannot be distinguished from *hepatic metastasis* from a silent primary focus elsewhere in the body.

The prognosis is hopeless

Enlargements of the Liver and Spleen. During examination of the abdominal viscera the spleen may be found enlarged Such enlargement may or may not be associated with enlargement of the liver Under the ordinary conditions of an examination by physical means a palpable spleen is significant. In many instances the enlargement of the spleen may be extreme and may be the first and only symptom of serious disease

The causes of splenomegaly are enumerated as follows: (1) infectious, (2) circulatory, usually mechanical in origin, (3) hemic and lymphatic, (4) metabolic and (5) cystic and neoplastic (see Chapter 12).

THE GALLBLADDER AND BILE DUCTS

THE GALLBLADDER

The gallbladder reaches the surface at the anterior end of the right ninth costal cartilage, just to the outer edge of the rectus muscle. This is the upper end of the right linea semilunaris Normally the gallbladder is not palpable. Many dubious claims are made in regard to the ability to palpate the distended gallbladder. However, at times, it can be palpated. *Hydrops* is the common cause for a palpable gallbladder.

Congenital and Acquired Anomalies and Malpositions. In the embryo which is 15 mm long the gallbladder is represented by an elongated mass. The bile ducts already have patent lumina The bile ducts and the lumen of the gallbladder develop by a process of vacuolation If vacuolation is disordered structural defects or congenital absence of the ducts or gallbladder may result Splitting, as an aberration of vacuolation, may produce a double, a bilobate, or an hourglass gallbladder, or a diverticulum of the gallbladder

Agenesis or absence of the gallbladder is a rare condition which occurs twice as frequently in women as in men. Absence of the gallbladder is compatible with digestive comfort.

Anteroposterior bends in the developing gallbladder are situated at the distal end and at the junction between the body and the fundus. The latter fold normally disappears, but when it persists, it participates in the formation of a folded-fundus gallbladder or *phrygian cap* The phrygian cap does not interfere with function of the gallbladder

There are two varieties of *double gallbladder*· one in which each duct empties independently into the same part or different parts of the extrahepatic biliary duct system, and one, the lambda type, in which the two ducts open into a common cystic duct The vesicles may appear as two distinct organs at variable distances apart or may be invested with a common peritoneum.

The *bilobate gallbladder* consists of a completely divided gallbladder with a common cystic duct.

Acute perforation of the gallbladder usually is preceded by an obstruction by a stone of the cystic or the common bile duct which produces distention of the gallbladder and interference with circulation of the blood, and gangrene ensues. The wall of the gallbladder, weakened by gangrene, ruptures. Occasionally there is thrombosis of the cystic artery, and sudden rupture follows A rare cause of rupture of the gallbladder is bacterial infection which weakens the wall of the gallbladder, as in typhoid fever.

Perforation of the gallbladder usually occurs at the fundus It is found in persons from 40 to 60 years of age. A history of previous attacks of cholecystitis is generally recorded unless the perforation occurs secondary to atherosclerosis or an infection.

The symptoms of acute free perforation in a patient who has acute cholecystitis are difficult to recognize until generalized peritonitis develops. There is pain in the right hypochondrium, in the epigastrium, or in the right lower abdominal quadrant. The pain progressively increases in severity and in extent until it becomes generalized throughout the abdomen

On examination the pulse is rapid and fever is present. Shock and peripheral vascular collapse are prominent when bile peritonitis is present The abdominal wall is tense, and muscular rigidity, at first most marked in the right side of the hypochondrium, gradually advances so that the entire abdomen becomes involved Acute tenderness in the right upper and right lower abdominal quadrants becomes widespread as the peritonitis progresses Abdominal distention develops and may become prominent

Free perforation should be suspected in any patient who presents signs and symptoms indicating acute inflammation of the gallbladder, who has persistent pain, and who shows a progressive increase in the degree and extent of abdominal tenderness, rigidity and shock A correct diagnosis of free perforation is not usually made in acute cholecystitis

One half of the persons who die from acute cholecystitis have acute free perforation of the gallbladder The commonest causes of death after surgical operation for acute perforation of the gallbladder are peritonitis and pulmonary embolism An acute hepatic insufficiency with the added features of shock may develop and cause death

Bile Peritonitis. Among the known causes of bile peritonitis are perforation of the gallbladder, rupture of any of the bile ducts after surgical operation on the biliary tract, traumatic rupture of the bile ducts, leakage from injured accessory hepatic ducts in the bed of the gallbladder subsequent to cholecystectomy, and malignant invasion of the gallbladder or bile ducts with perforation

In some patients there are no objective findings which will account for the leakage of the bile This group of patients who have idiopathic bile peritonitis is sizable

There is often in the abdomen an increased amount of free fluid which varies in color from amber to light green The peritoneum is congested and is covered with numerous plaques of fibrinous or fibrinopurulent material Gallstones in the bile ducts or free in the abdomen have been reported in more than half of those who have perforation of the gallbladder

The manifestations are those of acute peritonitis

The diagnosis of bile peritonitis is seldom made The diagnosis of general peritonitis is usually made prior to operation or necropsy

The therapy of bile peritonitis is prompt operation [illegible] ule, repair of any perf [illegible]

The mortality [illegible] or absence of infectic [illegible] of illness prior to operation The average mortality rate is 50 per cent

Chronic Cholecystitis and the Calcified Gallbladder. If roentgenologic examination fails to reveal evidence of stone, impairment or loss of concentrating function, or pericholecystitis, the surgical removal of the gallbladder which has been

off, or the pain may recur every few hours. More often, a constant dull or severe aching pain may continue for several days.

The pain is situated in the right upper quadrant of the abdomen in about one half of those who have it, and in the remainder the pain is in the epigastrium Reference of pain to the midscapular region or to the right infrascapular region occurs in approximately one half of these patients. In some the pain is referred to the shoulder tip, in others, to the left upper abdominal quadrant, or to the loin.

Chills or chilly sensations may occur at the onset of an attack. The temperature may be within the limits of normal or rarely exceeds 100 F (37.8 C)

EXAMINATION On examination, abdominal distention of variable degrees is present in about 1 of every 5 of those who have acute cholecystitis From time to time severe ileus (the so-called gallbladder ileus) may attend the acute pain, with great distention of the abdomen. There is tenderness in the right upper quadrant of the abdomen. Also, tenderness may be elicited by jolting the lower margins of the ribs on the right side of the back In mild attacks the patient may be aware of tenderness on deep inspiration or on descending a stairway. In an occasional patient a tense, tender, distended gallbladder or a tender mass may be palpated in the right upper portion of the abdomen

Jaundice can be detected in about 1 of every 4 during the acute phase of cholecystitis Jaundice may occur in association with acute cholecystitis without there being a stone in the common duct

The leukocyte count may be increased. In about 1 patient of every 5 the count will exceed 15,000 cells per cubic millimeter of blood A single leukocyte count is a poor index of the character and extent of the associated pathologic process in an acutely inflamed gallbladder The general trend of several counts is a useful indication in following the progress of the disease

The erythrocyte sedimentation is increased

The routine determination of serum-bilirubin concentration is of some value *Small degrees of hyperbilirubinemia are not diagnostic of stones in the common* duct Serum-bilirubin concentrations as high as 3 mg per 100 ml are often observed during the course of acute cholecystitis in the absence of a stone in the common duct.

There is usually *bile* in the urine Glycosuria which appears for the first time during an attack of acute cholecystitis may indicate a participation of the pancreas in the process.

DIAGNOSIS A sudden onset of nausea, vomiting, and acute, mild or severe pain in the upper right abdominal quadrant, going through to the back, occurring in a *patient about 40 years of age and overweight,* is *diagnostic* in most instances Often there is a history of previous attacks of pain which required hypodermic injections of opiates for relief.

Among the common disease conditions which may produce similar symptoms are acute appendicitis, subacute perforation of a peptic ulcer, and renal colic.

If jaundice becomes prominent, there is usually a *stone in the common duct*

The patient who has the manifestations of peritonitis, or fever, rapid pulse, marked leukocytosis and a large, tender gallbladder suggesting imminent *perforation,* should be operated on promptly If there is jaundice and the forementioned symptoms are mild or absent, it may be well to postpone surgical treatment until the patient can be properly prepared for operation

Even in the presence of mild symptoms, diagnostic studies are postponed until all signs of acute inflammation have subsided

Acute Perforation of the Gallbladder. Acute free perforation of the gallbladder is found at the time of operation in 1 of every 200 cases of gallbladder disease in which surgical exploration is made. Of the perforations of the gallbladder which occur as complications of acute cholecystitis, about 1 of 4 is free.

symptoms. This incidence of symptoms does not include dyspeptic symptoms occurring day after day in those who have, and those who do not have, uncomplicated cholelithiasis Symptoms of gallstones must be limited to the syndrome of gallstone colic or biliary colic This syndrome is characterized by attacks of pain indistinguishable from the pain in the presence of acute cholecystitis. The pain increases and decreases slowly in intensity, it is not a true colic. The belching associated with "gallbladder dyspepsia" is due to air swallowing, overeating, anxiety, fear and tension. It is not due to gallbladder disease and it will not be relieved by removal of the gallbladder. It may be relieved for a while after the gallbladder is removed, but will return as soon as the patient returns to her regular daily routine and becomes tense The so-called qualitative food distress of gallbladder disease, for instance, an intolerance of fats, fruits and uncooked vegetables, is commonly associated with an accompanying psychoneurosis. However, these symptoms may be due to gallbladder disease A patient who has headache followed by nausea and vomiting often attributes the complaint to biliousness Bilious attacks should not be presumed to be due to gallbladder disease Often so-called bilious attacks are accompanied by vomiting and retching After retching, a pain and soreness may appear in the upper part of the abdomen. Such soreness and pain, as described by the patient, are very much like the discomforts of biliary colic. Often the so-called bilious attacks are migraine. Migraine is not relieved by cholecystectomy

The most important genuine symptom to be related by the patient who has gallstones is the change of color of stools and urine, the stools being lighter than normal, and the urine very dark Of more significance than the color of the urine is the history of the passage of light-colored feces, for the color of the urine may be deepened by concentration of the urine, which may be the result of dehydration caused by abstinence from food or drink and by vomiting A slight transient icterus may occur from many causes, but when it follows biliary colic it is usually due to acute cholecystitis and stone in the cystic duct or in the common duct

Examination The patient who has gallstones often has not had symptoms. Therefore the results of abdominal examination are negative for evidence of the cholelithiasis If the patient is examined during an attack of pain, the findings are the same as those during an attack of acute cholecystitis. There are tenderness and often muscle guarding in the right upper part of the abdomen The results of examination shortly after such an attack may be negative Often there is residual tenderness, however, which may be elicited over the upper right abdominal quadrant or by light pounding with the ulnar side of the hand over the back.

Diagnosis The diagnosis of gallstone disease often can be made with a reasonable degree of accuracy from the history and the findings on physical examination If jaundice attended the attack of pain, the diagnosis can be made with more certainty A diagnosis of gallstones without confirmation by positive roentgenologic examination is rarely necessary

The important complications of cholelithiasis are empyema, gangrene and free perforation of the gallbladder, pericholecystic abscess, hepatitis, cholangitis, pylephlebitis and septicemia The common complication, which is often important because of its frequency, is jaundice

Any patient who has had an attack of biliary colic in association with jaundice or without jaundice, and who has demonstrable gallstones on roentgenologic examination, or any patient who has had such an attack who has a nonfunctioning gallbladder, proved by the usual technic of roentgenologic examination of the gallbladder, should undergo cholecystectomy. Any patient who has gallstones and evidence of impairment of liver function may be considered for cholecystectomy. The occurrence of manifestations of cardiac dysfunction following the onset of symptoms of cholelithiasis requires consideration for removal of the gallbladder.

clinically diagnosed as having chronic cholecystitis usually will not give lasting relief from the subjective complaints.

In contrast to the gallbladder which does not contain stones is the calcified gallbladder which may be causing symptoms. Calcium may be diffusely deposited throughout the gallbladder or it may occur in discrete patches Calcified gallbladders are often enlarged and functionless, and may be associated with obliteration of the cystic duct.

A calcified gallbladder may be proved to be nonfunctioning by roentgenologic examination A nonfunctioning gallbladder is significantly diseased. If the gallbladder is functioning and free from stones, and only a primary shadow is present in the roentgenogram, the gallbladder is not significantly diseased.

Cholelithiasis. Gallstones vary greatly in size and number Although most stones in a gallbladder seem to be of a single age, stones of different ages may occur

Calculi are found with great frequency in both the gallbladder and the common duct They rarely are confined to the intrahepatic ducts, but when so confined, the stones are almost always the black so-called pigment (bilirubin-calcium) stones

The exact mechanism of the genesis of gallstones is unknown The predisposing factors of gallstone formation are (1) metabolic, (2) chemical and (3) local.

During the last trimester of pregnancy the intra-abdominal pressure interferes with the outflow of bile It has been postulated that the biliary stasis thus created in pregnancy may be a factor in the production of gallstones. Postulations associating the formation of gallstones to endocrine disturbances have been made without good evidence that such occurs

It has been demonstrated that bile salts are concerned with keeping cholesterol in solution The precipitation of cholesterol occurs whenever there is significant lowering of the bile-acid content in the gallbladder in proportion to the cholesterol The normal gallbladder acidifies hepatic bile and perhaps in this way prevents calcium carbonate and other ingredients of gallstones from precipitating Any factor which alters the normal acidification of bile in the gallbladder is concerned in gallstone formation

It seems probable that infection and associated inflammatory changes within the gallbladder may be secondary to interference with gallbladder function brought about by mechanical obstruction of the cystic duct or the common duct, or both, by the calculi Infection, however, usually is not a major factor in the genesis of most gallstones, pathologic changes in the gallbladder, like the infection, are secondary to the presence of stones, the stones having been formed by aberrations in normal chemical reactions which maintain the constituents of bile in solution

No direct relation has been established between the concentrations of cholesterol in blood and in bile in the obese who have gallstones.

Repeated attacks of acute or subacute cholecystitis originated by stones eventually cause severe inflammatory changes in the vesical wall, which may become thickened and contract firmly on the contained stones The inflammation extends and there is pericholecystitis with adhesions to the liver, duodenum, hepatic flexure of the colon or omentum. Choledocholithiasis occurs in approximately one fourth of the cases of cholelithiasis Of rare occurrence are fistulas of the biliary tract, and the passage into the intestine of a stone or stones which obstruct the intestine Pancreatitis is a frequent complication of cholelithiasis

The recorded incidence of gallstones is mainly determined by the presence of symptoms, but since symptoms are often absent, estimates of the incidence are worthless

The occurrence of cholelithiasis with symptoms is commoner among middle-aged women than among men, and it steadily increases with age. However, gallstones do occur in infants, children and young adults In these a common cause is congenital hemolytic, or some other form of hemolytic, anemia. All races of men and many species of animals have gallstones

SYMPTOMS. Despite the dubious origin of the figures on the incidence of gallstones, it may be stated that about 1 in every 10 patients who have calculi has

digestive health after the gallbladder has been removed Likewise the postcholecystectomy syndrome does not affect those who have strictured common bile ducts or stones in the common bile duct which were not removed at the time of removal of the gallbladder.

The gallbladder is not a nuisance organ like the appendix, for it does have functions. However, these functions can usually be dispensed with, without manifest discomfort, as evidenced by the 9 of every 10 patients who have the gallbladder removed and are comfortable thereafter so far as the loss of the gallbladder is concerned

The gallbladder has two main functions. (1) It regulates bile pressure in the bile ducts by serving as an overflow reservoir and tension bulb. (2) The contraction of the gallbladder is regulated by the neuroregulatory mechanism which controls opening and closing of the sphincter. Postcholecystectomy syndromes may be associated with loss of these functions or may develop secondarily to a loss of the biochemical properties of the concentrated gallbladder bile

When the tension-regulating mechanism of the gallbladder which amounts to 150 to 200 mm of water is lost, the unchecked changes of bile pressure during active digestion may give rise to feelings of fullness, pressure, and cramplike pain resembling gallstone colic in the right upper quadrant of the abdomen The diameter of the lumen of the common bile duct is a factor in the production of these symptoms, for patients who have cholecystolithiasis without involvement of the common duct are much more likely to have symptoms than those patients who have had ampullar obstruction (Pribram) with dilatation of the common bile duct.

The postcholecystectomy syndromes which have been enumerated by Pribram are as follows (1) the pressure syndromes due to the missing tension-bulb function of the gallbladder and their secondary complications, cholangiohepatitis and pancreatitis, (2) the lowered tolerance for food, especially fatty food, due to the missing digestive aid of concentrated gallbladder bile and the hormone secreted from the wall of the gallbladder, (3) paralysis of the sphincter, leading to diarrhea and enteritis.

As a result of studies of the alteration of intraductal pressure after cholecystectomy, it has been agreed that the pressure may rise from 25 mm of mercury to 50 and 55 mm The influence of drugs on the changes of pressure in the common duct due to contraction of the sphincter has been studied by McGowan, Butsch and Walters and by Doubilet and Mulholland. It was observed that injections of morphine cause contraction of the sphincter followed by an increase of intraductal pressure from 150 to 200 mm. of water to 250 to 300 mm Antispasmodics like atropine cause the pressure to drop or at least prevent a rise in pressure after simultaneous administration of morphine. Inhalation of amyl nitrite produces a relaxation of the sphincter with an immediate drop of intraductal pressure Spasm of the sphincter does not cause pain The region of the sphincter [illegible]
duct
quie

entirely due to the *increased intraductal pressure* Among the complications related to the increased intraductal pressure and stasis of bile is *cholangiohepatitis*

Bile pressure and stasis of bile due to spastic conditions of the sphincter may increase after removal of the gallbladder, and cholangiohepatitis, not present before operation, may ensue Similar conditions prevail in the development of certain forms of *pancreatitis*

However, there are cases in which pancreatic conditions related to disease of the biliary tract disappear after cholecystectomy Reflux of bile into the pancreatic duct constitutes only one and probably not even a common cause in the pathogenesis of pancreatitis

The gallbladder concentrates bile, which increases its digestive aid It secretes a hormone-like substance (cholecysmon), a coenzyme which activates the fat-

The Nonfunctioning Gallbladder. The roentgenologic examination, when properly performed, may not reveal evidence of the presence of a gallbladder. If the gallbladder has not been surgically removed or has not been transposed through error in development to a place in the liver away from its usual situation, the absence of its shadow on the roentgenogram is significant The absence of the gallbladder on the roentgenogram is reported as a nonfunctioning gallbladder

A nonfunctioning gallbladder in a patient who has symptoms and findings of gallbladder disease usually contains calculi which are not radiopaque. The report of a nonfunctioning gallbladder is one of the most positive of radiologic findings.

The Primary Shadow. The gallbladder may cast a shadow on the roentgenogram without the administration of a radiopaque substance. Such a shadow has no particular diagnostic significance

Calculi in Dilated Stump of the Cystic Duct. After cholecystectomy the cystic duct may be dilated A pouch thus formed may vary from 1 to 2½ inches (2.5 to 6 4 cm) in length and may be of an average caliber of the little finger and contain stones within the dilated stump Peterson has recorded 42 such instances He considered the term re-formed gallbladder a misnomer and correctly concluded that the so-called re-formed gallbladder was the dilated stump of the cystic duct. In his experience the stump of the cystic duct assumed a shape like that of a normal gallbladder but, except in rare instances, was much smaller. It contained mucosa like that of the cystic duct with, in some cases, mucosa in the fundus suggestive of origin from the gallbladder. Its wall showed inflammatory signs Its lumen often contained stones. On histologic examination the excised structures were reported as showing chronic cholecystitis

Painful seizures which are either identical with or very similar to those experienced prior to cholecystectomy may occur Roentgenograms give positive evidence

Postcholecystectomy Syndromes. There is a group of clinical syndromes which with or without good reason have been attributed directly or indirectly to some missing functions of the gallbladder and which therefore have received the name postcholecystectomy syndromes

The relief of symptoms of biliary colic after cholecystectomy occurs in 9 of every 10 who have the operation if the diagnosis is correctly made, and proved by operation This statement is made with the assumption that the diagnostician and the surgeon are aware that aerophagia and, to a large extent, the so-called qualitative food distress often associated with gallbladder disease are not a part of the *syndrome of biliary colic* Aerophagia and qualitative food distress have as their origin psychoneurosis and not gallbladder disease.

Cholecystectomy performed for chronic cholecystitis without gallstones results in failure to obtain symptomatic relief in a number of patients Patients who have little or no relief of symptoms after cholecystectomy may have undergone operation because there was nonvisualization of the gallbladder on roentgenograms following the single-dose oral administration of the dye which may have been vomited A lesser number have been operated on because the gallbladder did not empty after a fatty meal Some of these patients are psychoneurotic individuals and removal of the gallbladder will not alleviate their discomforts

However, the 1 of every 10 who have had the gallbladder removed for gallstones and biliary colic who does not obtain relief will usually be found to have (1) calculi in the biliary duct, or common bile duct, (2) stricture of the common bile duct, (3) stones in remnants of the cystic duct or in remnants of the *gallbladder* [illegible] or (4) chronic cholangitis, which may [illegible] biliary colics and jaundice, and [illegible] the latter group of patients may have a chronic pancreatitis or pancreatic stones

It is emphasized that 9 of every 10 patients who undergo cholecvstectomy enjoy

stones are not present. Many of these gallbladders, however, contain stones which cause the symptoms for which the patients are submitted to surgical operation

The roentgenologic findings are not conclusive The diagnosis is made on opening the resected gallbladder.

Torsion of the Gallbladder. In rare instances the gallbladder is completely surrounded by peritoneum and has a mesentery-like attachment to the liver. In still rarer instances the gallbladder lies completely free except that it is attached to the liver through a pedicle composed of the cystic duct and its attendant structures. It is the pedicellate gallbladder which becomes twisted; torsion takes place. The condition is commonest in old women

The onset of symptoms is sudden The pain is constant and severe, and is like the severe pain of biliary colic Vomiting is present and sometimes is extreme Jaundice is variable but generally is absent. About 48 hours after the onset, there are fever, fast pulse and exhaustion, these may be the first indication of the seriousness of the disease in the aged patient

The abdominal wall is ordinarily rigid and there is distinct local tenderness over the region of the gallbladder There are no palpable masses

Tenderness over the gallbladder increases after about 48 hours The abdominal signs indicative of peritoneal irritation become more pronounced with increasing rigidity and more widespread involvement of the abdominal wall. The leukocyte count tends to increase and a pronounced leukocytosis may develop.

Diagnosis of torsion of the gallbladder cannot be made clinically. The usual preoperative diagnosis is cholecystitis

Torsion of the gallbladder requires immediate cholecystectomy. The prognosis is good

Tumors of the Gallbladder. Walters found *papillomas* in 8 per cent of the gallbladders which he removed. Small papillomas are often found in association with cholesterosis Large papillomas are rare. They may be pedunculated and all are benign

Adenomas are second in incidence to papillomas Adenomas occur singly and may be cystic, papillary or semisolid *Myomas, lipomas, myxomas* and *mixed types* have been occasionally reported *Fibromas* occur very rarely

Benign tumors are usually symptomless

The roentgenologist regularly diagnoses the papillomas correctly These tumors are not usually treated The other benign tumors are not diagnosable except by histologic study

Malignant Tumors. *Primary Carcinoma.* Primary carcinoma of the gallbladder is rare Often it is first discovered at necropsy It more commonly occurs in those who have gallstone disease

The relationship of carcinoma of the gallbladder to antecedent gallstones is not understood, for there is a very low incidence of carcinoma in the total number of patients who have cholelithiasis

The sex incidence shows a ratio of women to men averaging about 4.1. Women of 60 to 70 years of age may be affected, rarely men of these ages are affected.

Carcinoma is the common malignant tumor of the gallbladder Histologically there are adenocarcinomas and squamous cell carcinomas of the gallbladder. These tumors metastasize early to the regional lymph nodes and to the liver. The liver is the commonest seat of extensive secondary growth The colon, duodenum, stomach or jejunum may become involved by virtue of adhesion and subsequent extension of cancerous cells by contiguity Perforation of the carcinomatous gallbladder directly into these organs is common.

There is often a history of biliary colic which commences after the development of the cancer in those who do not have gallstone disease. In those who have gallstones too, a long history of biliary colic may be obtained.

Pain in the region of the gallbladder is more constantly present in carcinoma

splitting lipases. Concentrated bile with its salts is an important aid in the digestion of food. Bile salts activate digestive enzymes, form conjugated products with poorly soluble and therefore poorly absorbable substances, and help the latter to pass through the intestinal wall into the blood and lymph stream The bile salts act as catalysts both in the breaking down and in the absorption of foodstuffs. The gallbladder empties the highly efficient concentrated bile by active contraction in response to the stimulation of food during digestion and the formation of cholecystokinin in the intestines. The lack of these biochemical functions in cholecystectomized patients may well account for the observed *lowered tolerance for food,* especially fatty food.

With removal of the gallbladder the nervous plexuses of its serous and muscular wall also are removed These nervous plexuses control the opening and closing of the sphincter. The reflex of the sphincter after cholecystectomy may become uncontrolled or disorderly and dyskinetic disorders may ensue Dyskinetic disorders and spasm may not have been present before operation, but after cholecystectomy they may greatly aggravate the pressure syndromes

Spastic contraction of the sphincter following cholecystectomy occurs in only a few patients In others a pronounced atony or even a complete paralysis follows the removal of all of the nervous plexuses when cholecystectomy is performed Judd and Mann, in measuring the intraductal pressure after cholecystectomy, recorded in some instances, following an initial rise, a gradual diminution of pressure to zero, indicating the development of total paralysis of the sphincter This means a continuous drainage of bile into the duodenum instead of the rhythmic and interrupted emptying regulated by a functioning sphincter and related to the contraction of the gallbladder Continuous drainage of bile into the duodenum, particularly when the patient is in a fasting state, may be followed by diarrhea. Such diarrhea may be due to the purgative effect of the excess of bile salts pouring continuously into the duodenum

It is well to mention that postcholecystectomy syndromes occur commonly in young women who have a pronounced irritability of the digestive apparatus, hyperacidity and constipation There is a low incidence of postcholecystectomy syndromes when the patient really needs to have the gallbladder removed. There is low incidence of postcholecystectomy syndromes in complicated cases, and relatively high incidence in cases in which cholecystectomy has been performed in the presence of a mildly diseased and still somewhat functioning gallbladder.

Examination There are no findings either on physical examination or on roentgenologic studies which are characteristic of a postcholecystectomy syndrome

Diagnosis The diagnosis can be established only by time and observation and the exclusion of all other possible organic diseases. Many of these patients have all of their digestive complaints labeled by the surgeon, after the gallbladder has been removed, as being of neurotic origin Diets low in fat content with small meals and weight reductions if overweight may be helpful in improvement of the general health The asthenic, sitophobic patients may be helped by encouraging them to eat regularly and to partake of sufficient amounts of food to improve the general health

Milk of Calcium Bile. Milk of calcium bile (limy bile) is a rare condition due to deposition of lime salts within the gallbladder The symptoms are the same as those produced by gallstones Roentgenologic study is diagnostic The treatment is cholecystectomy.

Cholesterosis of the Gallbladder. Strawberry gallbladder is a term chosen by MacCarty to describe the gross appearance of the mucosa in advanced cholesterosis or lipoid gallbladder. Strawberry gallbladder is much commoner in women than in men

There are no definite symptoms caused by cholesterosis of the gallbladder if

A biliary obstruction in association with choledocholithiasis often initiates cholangitis. Suppurative cholangitis is but a further stage of cholangitis and seldom can be diagnosed prior to death

Acute cholangitis and suppurative cholangitis are suspected but not diagnosed if recovery ensues If death follows, a diagnosis is made at necropsy.

Chronic Cholangitis. The term cholangitis lenta describes a type of chronic infective nonsuppurative cholangitis which involves the intrahepatic bile channels, is due to infection with the streptococcus (usually a viridans strain), and often is associated with, or actually causes, endocarditis. Chronic low-grade icterus and swelling of the liver and spleen together with intermittent fever are present in association with the bacterial endocarditis.

The prognosis is bad even if antibiotics are correctly used.

Choledocholithiasis. Judd and Marshall recorded 5.5 per cent of gallstone disease restricted to the common duct. In 25 per cent of all cases of gallstone disease there are stones in the common duct. A ductal origin of calculi can occur but it must be rare as compared to origin in the gallbladder. The presence of the calculi in the ducts is more correctly explained as due to a migration of calculi from the gallbladder.

In about 4 of every 5 patients who have choledocholithiasis the gallbladder is diseased, and often it is fibrotic and functionless (Walters and Snell). Hepatic damage is a frequent concomitant, slight to moderate damage is mentioned in about two thirds and marked structural hepatic changes in about one third of the reported cases of obstructive jaundice caused by stones in the common duct (Snell). Chronic inflammatory changes with fibrosis are to be seen in the pancreas in about 25 per cent of persons who have choledocholithiasis. Pylephlebitis and thrombosis of the portal vein are encountered rarely The age and sex incidence are the same as for stones in the gallbladder.

Stones present in the common bile duct have passed into the duct from the gallbladder and have entered it through the cystic duct. The manifestations of stones in the common duct are the same whether the gallbladder has or has not been removed In Weir's experience with common duct stones the asymptomatic period following removal of the gallbladder averaged 3 years and 8 months. Often there is a feeling of epigastric distention and pain. In one half to two thirds of patients suffering from common duct stone the pain is referred to the back. In an occasional

the common duct, chills and fever rarely occur in the latter if jaundice is present However, a stone in the common bile duct in the presence of a hepatitis may be associated with recurrent chills and fever, generalized aches and pains, progressive anemia, jaundice and enlargement of the liver In these patients the manifestations due to a stone in the common duct are very much the same as those of chronic cholangitis.

A stone present in the common duct without jaundice is termed a silent stone.

The liver is often palpable and tender. If obstructive biliary cirrhosis, as the result of long-standing jaundice, is present, the spleen is enlarged and palpable, and in a few who have palpable spleens there will be ascites During and for a short time after an attack of colic there is tenderness in the right upper quadrant of the abdomen. In rare instances the gallbladder will be palpable if it has not been removed.

A diagnosis is based on the findings at operation, a stone in the common bile duct or stone in the extrahepatic ducts, with removal of the calculus

of the gallbladder than in biliary colic. The pain is often followed by jaundice, loss of body weight, vomiting, anorexia and weakness.

In about three fourths of all of those who have cancer of the gallbladder examination reveals a palpable, hard, tender tumor which seems to be a part of the liver Jaundice usually is continuous, although intermittent jaundice may occur. The jaundice results from obstruction of the common duct Fever is present sometime during the course of the illness Ascites is often a late development

The diagnosis is not established prior to operation or necropsy.

Primary Sarcoma Primary sarcoma in the gallbladder is extremely rare Clinically there are no features which serve to distinguish between sarcoma and carcinoma of the gallbladder However, sarcoma may occur in younger patients than carcinoma

DISEASES OF THE BILE DUCTS

Anomalies and Abnormalities of the Common Bile Duct. The main portion of the hepatic diverticulum elongates into the ductus choledochus and hepatic ducts Bile ducts within the liver arise secondarily, beginning in the embryo at 8 weeks The main ducts are subject to agenesis, duplication and sacculation.

The common bile duct may open into the stomach near the pylorus, or join the duodenum independently of the pancreatic duct The common bile duct may be duplicated, so that two separate ducts enter the duodenum or one branch may enter the duodenum and the other enter the stomach

The bile duct may be dilated, and associated with a choledochus cyst Often choledochus cysts are associated with partial or complete obstruction of the common duct These cysts are retroperitoneal, either ventral or dorsal to the duodenum They are usually small, but may reach a capacity of several liters. The gallbladder is of normal size or smaller than normal

Agenesis is a rare abnormality of the common duct In agenesis the duct or ducts may be absent or may be represented by a fibrous cord Frequently icterus is present at birth or it appears within 48 hours Eventually, about the second month, a diagnosis of obstructive jaundice is made

The cystic duct may join the hepatic duct in devious ways For instance, it may join the hepatic duct at an angle, run parallel with the hepatic duct and be enclosed in the same sheath before joining it, or it may seem to circle around the duct

Cholangitis (Catarrhal Jaundice) Bacterial inflammations of the biliary passages are secondary to disease of the gallbladder, liver, pancreas or adjacent structures Inflammations of these structures are either acute or chronic. They often produce a truly catarrhal

If there is an appearar

swelling and tenderness of

of any disease of the biliary passages, gallbladder, liver or pancreas, cholangitis is suspected as the cause

Viral infections are responsible for the occurrence of epidemic hepatitis, which is unrelated to the catarrhal jaundice enumerated here The presence of bacteria in the biliary passages has no pathogenic significance and usually does not give rise to disease of the biliary tract Infectious cholangitis may be either enterogenous or hematogenous in origin In cholangitis of the enterogenous type, the organisms most frequently recovered are *Escherichia coli, Salmonella typhosa* and *Salmonella paratyphi*

In hematogenous cholangitis the commonest causative organisms are those which often are present in septicemia, for instance, *Streptococcus viridans, Streptococcus hemolyticus, Staphylococcus aureus,* pneumococci, Friedlander's bacilli and influenza bacilli The commoner acute infections accounting for these organisms are tonsillitis, appendicitis, pneumonia, diphtheria and typhoid fever For these acute infections to be of etiologic significance the cholangitis must occur during the active infection or immediately thereafter.

stricture. The onset of obstructive jaundice due to stricture occurring late after operation is insidious. There are fever, jaundice, and often enlargement of the liver and the spleen.

The diagnostic procedures are the same as those employed in diagnosis of stones in the common duct However, the diagnosis is never certain until proved by surgical exploration

Strictures at the Ampulla of Vater. Obstructions and strictures of the common bile duct at the ampulla or the sphincter of Oddi are usually attributed to stone or spasm, but may be due to fibrosis at the papilla Fibrosis of the bile duct at or near the sphincter of Oddi appears to be a disease mainly of patients from 50 to 70 years of age. The characteristic manifestation is an obstructive type of jaundice, the cause of which, prior to operation or necropsy, is not recognizable or distinguishable from any other cause of an obstructive jaundice.

Biliary Fistulas. Biliary fistulas usually are complications of gallstone disease or of surgical operation for gallstones Less frequently there is empyema of the gallbladder with formation and drainage of abscess All biliary fistulas are rare, but spontaneous external fistulas and postoperative internal biliary fistulas are very rare.

The persistence of an external biliary fistula after operation is manifested by persistence of acholic stools after the tube inserted in the ducts by the surgeon for the drainage of bile, has been clamped prior to its removal or by persistence of copious drainage of bile from the sinus tract after removal of the tube for bile drainage Cholangiography performed before the removal of the drainage tube enables detection of the cause for persistence of acholic stools or the loss of large amounts of bile externally and the situation of fistulas if they are present.

Balfour and Ross pointed out that the commonest cause of external biliary fistula is incomplete surgical intervention or injury to the biliary tract at the time of operation

Under normal conditions, after the removal of a drainage tube from the common duct, bile flow should cease within 10 days

In most instances an external fistula of the gallbladder which is draining mucus is due to obstruction to the cystic duct by a stone or by chronic inflammation This condition is easily recognized and is completely remedied by cholecystectomy.

After cholecystostomy, if there is continued drainage of bile from the gallbladder and if little or no bile enters the intestinal tract, a stone usually is present in the common duct However, malignant lesions obstructing the terminal bile duct may be present.

Practically all of the bile secreted may be drained off for a long period without the development of a serious deficiency state In infection of the biliary tract and secondary hepatitis, nutritional deficiencies develop more rapidly because of a lack of the action of bile in digestive processes In these patients there may be an associated osteoporosis, avitaminosis, electrolyte imbalance, and disturbances in water and salt metabolism.

[illegible] *ulas* are biliary-duodenal,

[illegible] oduodenal, is found as a sequela of acute cholecystitis with empyema, involving the gallbladder containing stones A less common cause for [illegible]

[illegible]

The sequence of symptoms of choledochoduodenal fistulas is obstructive jaundice, with the disappearance of the jaundice after a severe attack of pain. The presence of a choledochoduodenal fistula in a patient who has not had antecedent jaundice should suggest the possibility of a primary duodenal lesion

Rapid loss of weight, chills, fever, and severe diarrhea are often present in

After cholecystectomy for cholelithiasis, recurring colics and jaundice are strong evidence for a stone in the common duct. A persistent biliary fistula following drainage of the gallbladder for stones is good enough evidence for a presumptive diagnosis of stone in the common duct.

Plain roentgenograms of the right upper quadrant of the abdomen may reveal calculi in 1 in every 7 cases. In cholecystectomized patients the frequency with which opaque calculi in the region of the ducts are disclosed by a plain roentgenogram is small

Treatment of common duct stone is surgical removal.

Rupture of Bile Ducts. Infection after surgical operation or infection alone or infection associated with the reflux of activated pancreatic juice in the absence of stone may cause rupture of the common bile or hepatic ducts. Rupture of bile ducts may also result from a blow to the abdomen or from a puncture wound

During the immediate postoperative period after operation on the biliary tract, perforation of the bile duct may be suspected if bile appears around the external drain The occurrence of spontaneous rupture of the bile ducts late after operation may not be recognized.

The symptoms of rupture of a bile duct or ducts may resemble those of an acute freely perforated peptic ulcer

Stricture of the Common Bile Duct. Cicatricial stricture of the common bile duct occurs as the result of gallstone disease and from a benign fibrotic process of unknown origin The stricture occurring as the result of gallstone disease is primarily traumatic or inflammatory in origin Traumatic strictures occasionally but rarely follow surgical injury to the common bile duct

Stricture of the bile ducts in the absence of gallstone disease or operative trauma occurs. Stricture of this type appears well away from the sites liable to direct surgical trauma, which lends credence to the belief that these strictures often occur primarily and independently of surgical trauma

The symptoms of primary acquired inflammatory stricture of the common bile duct may be indistinguishable from those of tumor of the main bile duct or the head of the pancreas. The incidence of carcinoma of the pancreas which causes obstruction and jaundice is much greater than that of cicatricial stricture of the common duct. This increased incidence of carcinoma of the pancreas over that of carcinoma of the common bile duct is diagnostically helpful when obstructive jaundice is present in the absence of calculi.

The conditions which predispose the common bile duct to stricture following surgical intervention are anomalies in the origin and course of the cystic artery, such as a long cystic artery coursing parallel to the common bile duct or an abnormally short cystic duct Probably a commoner cause for accident during surgical operations is obliteration of anatomic landmarks, interfering with identification and exposure of the ducts during operation (Walters)

Jaundice is the characteristic manifestation of postoperative occlusion of the common bile duct. If complete occlusion of the common duct occurs at the time of cholecystectomy, jaundice occurs within 12 to 48 hours If jaundice does not appear until several days after operation and is associated with a fever, there is an infection from leakage of bile from an injured duct, or soiling from an acutely inflamed gallbladder, or a stone remaining in the common duct Spastic closure of the papilla of Vater is rare, but when it is responsible the jaundice clears within a few days to a [illegible] and progres-

[illegible] t be mani-

[illegible] truction of

[illegible] biliary ducts occurring later than 6 months after operation on the biliary tract is rarely due to stricture unless more than one operation has been performed for

purative cholangitis develop Pericholangitic fibrosis and changes characteristic of obstructive biliary cirrhosis have been described

The commonest sites of metastatic spread are the liver, regional lymph nodes, pancreas and lungs.

The onset is usually insidious, with jaundice. Progressive obstructive jaundice and loss of body weight are the usual manifestations There may be present pain, pruritus, anorexia, fever, vomiting, dyspepsia and constipation or diarrhea

A preoperative diagnosis of a tumor of a biliary passage is not essential. Mechanical obstruction of the main bile duct requires surgical operation. The diagnosis is established by biopsy at the time of operation

FUNCTIONAL DISORDERS OF DIGESTION

A functional disorder of digestion implies a physiologic disturbance not due to any known primary structural changes. There is no general agreement on this concept, however, since the scope and limitations of functional disturbances cannot be defined and, more particularly, since often a clinical distinction between what is functional and what is structural cannot be made

Disturbances of function occurring in association with or subsequent to proved organic diseases of the gastrointestinal, respiratory, circulatory, generative and urinary systems, or in conjunction with diseases of the brain and spinal cord, or in relation to various systemic infections, intoxications, and deficiency states, are not regarded as functional in nature unless such symptoms existed prior to the onset of the organic disease Physiologic disturbances which occur in relation to causes such as endocrine and metabolic disturbances are likewise not diagnosed as functional disorders

In a description of functional disorders of digestion it is necessary to consider the influence of the following conditions on digestion (1) heredity, (2) changes in the autonomic nervous system; (3) emotional conflicts; (4) personality, (5) anxiety, (6) hormones; (7) convalescent states from infections or other illnesses, physical fatigue, and infections, (8) the allergic state; (9) nonallergic foods; (10) laxatives, (11) motor disturbances; (12) the coexistence of gastrointestinal disease and psychoneurosis, (13) achlorhydria, (14) gastroenterostomy; (15) fecal impaction and (16) sprue (tropical and nontropical)

Heredity A *hereditary* tendency may be of significance. A full genealogic history may reveal a high incidence of similar digestive dysfunctions

Autonomic Nerves The terms vagotonia and sympathicotonia designate autonomic nerve imbalance Such oversimplicity in explanation of disease of the autonomic nervous system in relation to digestion has not proved to be of value in either diagnosis or treatment of disorders of the autonomic nervous system or of the digestive system

The intrinsic nerve structures of the intestines comprise the myenteric plexuses of Auerbach and the submucous plexus of Meissner, which are influenced by the two major divisions of the autonomic nervous system For instance, hypertonicity and increased peristalsis and spasticity of the sphincters follow increased vagal activity

Pain may originate in the gastrointestinal tract as a result of either overdilatation or overcontraction of hollow viscera, and from stretching of the capsules of the solid organs

Emotional Conflicts. In the evaluation and thus the diagnosis of digestive disease brought about by emotional conflicts or abnormal psychic tensions, it is well to recall that the principal relay station for emotional components of disease appears to be the diencephalon It is responsible for the correlation of psychic and somatic disorders. and it has a regulating influence on both of the major divisions of the

cholecystocolonic fistula. The patient has had symptoms of disease of the biliary tract, in which a more lasting severe attack is associated for the first time with diarrhea. Immediately following the onset of the diarrhea there is disappearance of the jaundice. Cholecystocolonic fistula often can be diagnosed by means of roentgenologic studies of the colon

Biliary-gastric fistula is commonly due to gallstone disease.

Bronchobiliary fistula is rare but develops as a complication of gallstones, echinococcus disease, and amebic abscesses of the liver or liver abscesses as a result of external trauma. The establishment of a bronchobiliary fistula commences with an acute exacerbation of chronic disease of the biliary tract or hepatic disease followed by an irritating cough with embarrassment to respiration. If these symptoms are followed by the expectoration of large amounts of bile, the diagnosis is established The usual physical signs characteristic of minimal basal pneumonitis, atelectasis or diaphragmatic pleurisy may be present

Roentgenologic examination may be diagnostic in all *internal fistulas* which communicate with the alimentary canal

The prognosis is usually poor in all types of biliary fistulas. It is good in those readily amenable to surgical resection and repair.

Functional Disorders of Bile Flow. Various terms have been used to describe functional disorders of bile flow They [illegible]
atonic dyskinesia, spastic and atonic d[illegible]
tonica, postcholecystectomy syndrome [illegible]

Biliary dyssynergia capable of causing symptoms occurs in patients who have had severe gallbladder disease or who have undergone surgical operation on the biliary tract

Often adequate roentgenologic survey of the biliary tract will disclose causes other than dyssynergia to explain the complaints Pains in the hepatic region occurring in association with gastrointestinal neuroses or profound derangements of the autonomic nervous system are not due to biliary dyssynergia

Tumors of the Bile Ducts. In the experience of Walters and Snell benign tumors of the bile ducts have little clinical importance They are exceedingly rare and are usually so small that they do not give rise to symptoms

Adenomas make up the greatest number of benign tumors, and many of these are described as papillomas Other rare benign tumors of the bile ducts include lipoma, fibroma, adenomyofibroma, neuroma and carcinoid tumor

Benign tumors of the bile ducts are rarely suspected clinically They are discovered either at surgical operation or roentgenologically. Symptoms, if present, simulate those of obstructive jaundice of other origins If colic, fever and jaundice are present, calculi are usually suspected.

Primary Malignant Tumors of the Extrahepatic Bile Ducts. Primary malignant tumors of the extrahepatic bile ducts are somewhat commoner than are benign tumors of these ducts These malignant growths occur oftenest in men between 50 and 70 years of age. They are not related to gallstone disease The most frequent sites are the common duct and the junction of the cystic and common hepatic ducts. There are three anatomic varieties, villous, nodular and diffuse The villous type is rare

According to Judd and Gray, the grade of malignancy in two thirds of cases observed by them was 3 or higher (Broders' classification on a basis of 1 to 4, in which 1 represents the lowest, and 4 the highest grade) [illegible] empyema [illegible] the duct [illegible] become enlarged and may be the seat of advanced hydrohepatosis Atrophy and necrosis may be noted in the hepatic lobules, usually confined to the central zones R[illegible]

goiter accounts for a very small number of instances in which there are symptoms of colonic neurosis

A low metabolic rate has been frequently observed in instances of functional digestive disorders of the colon. However, low metabolic rates (—10 to —20 per cent) are common in many who have various sorts of psychoneuroses without digestive complaints

Vitamin deprivations cause intestinal disorders.

Convalescent States, Physical Fatigue and Infections. Derangements of digestion simulating functional disorders may follow serious or inconsequential *bacterial and viral infections* and other irritants acting within the alimentary tract, or generalized infections such as those of the upper part of the respiratory tract

Infections within the alimentary tract may cause chronic diarrhea. It may be difficult bacteriologically to identify certain bacteria such as streptococci or *Clostridium perfringens* as the causative agents However, at times these may originate a chronic diarrhea Bacillary dysentery is an acute infectious disease of the intestines, but this infection may linger and cause a chronic diarrhea of several months' duration *Salmonella typhosa, Salmonella paratyphi, Salmonella schottmuelleri, Salmonella hirschfeldii, Salmonella typhimurium, Salmonella gallinarum* and *Salmonella pullorum* all may cause prolonged diarrheas. In some instances a gonorrheal proctitis may cause frequent bowel evacuations

Lymphopathia venereum infections often produce strictures of the rectum, and such strictures while ulcerated and secondarily infected may cause frequent emptying of the bowel Ordinarily lymphopathia venereum infections are associated with stricturing, constipation or obstipation

Tuberculosis of the intestine is a common bacterial infection associated with a chronic diarrhea

Syphilitic infections of the intestines are difficult to delineate, and certainly a chronic diarrhea cannot be attributed to syphilis.

Intestinal actinomycetes may infect the intestines and cause chronic diarrhea which may resemble that of tuberculosis Intestinal nocardiosis is less common The fungi imperfecti, except for *Candida albicans*, rarely originate disease *Candida albicans* is found in quantity in the stools of patients who have chronic diarrhea due to such causes as sprue and pernicious anemia. It would be difficult to prove that fungi imperfecti cause chronic diarrhea.

Histoplasma capsulatum may infect the intestine causing a chronic diarrhea resembling that observed in patients who have tuberculosis or actinomycotic infections

The protozoan parasites, *Endamoeba histolytica,* and the flagellates *Giardia lamblia, Trichomonas hominis* and *Chilomastix mesnili* may be associated with chronic diarrhea However, it is not diagnostically safe to assign any of these organisms for the cause of a chronic diarrhea except *Endamoeba histolytica* The infusorian, *Balantidium coli,* causes a serious acute colitis when the bowel becomes obstructed It is not a cause of chronic diarrhea

Infection with *Leishmania donovani* may be complicated by chronic diarrhea.

Helminthes usually do not cause diarrhea

The so-called special methods of isolating a particular intestinal bacterium and then testing the skin for hypersensitivity to this bacterium or its products, and the therapeutic results obtained by the treatment of intestinal disease by means of vaccines or the removal of foci of infection, are scientifically dubious procedures.

Physical fatigue and exposure to cold may be important causes of functional digestive attacks Weakness following long febrile illnesses or infections of the upper part of the respiratory tract may aggravate or initiate the symptoms of alimentary neuromuscular instability. A painful abdominal crisis may leave as an aftermath the irritable colon syndrome

autonomic nervous system which also centers there. The diencephalon also has direct influence on most of the endocrine glands, on metabolism as well as on all homeostasis. The diencephalon receives impulses from and sends impulses to the cerebral cortex In primary somatic disease the diencephalon receives abnormal impulses and registers them in the viscera, especially in the abdomen. Disorders in which there is either a lack or an increase of normal and abnormal constituents of the blood may affect the center directly or centripetally via the autonomic nervous system In states of emotional conflict and abnormal tension the diencephalon may be influenced from the cerebral cortex and then set up impulses *responsible for secondary changes in function* and even in structure of the viscera A consideration of these factors requires as criteria for diagnosis first, the absence of any primary physical or chemical changes, and, second, the finding of satisfactory psychologic causes to account for the clinical manifestations

In those who have functional gastrointestinal disturbances due to psychologic causes, there is a change of affect and this is termed the subjective phase There are often disturbances of the special senses such as sensations of appetite, hunger and pain The objective phase, due to psychologic disorders of digestion, includes disturbances in the neuromuscular, autonomovisceral, and secretory functions These disturbances are termed objective because they can be observed clinically

Personality. Changes in the affect are related to the personality of the patient In order to identify these disorders and to treat them satisfactorily, the physician is asked to have a basic concept of the structure of personality, types of personality, and the various types of reaction in relation to disease processes

The several personality reaction types include (1) the *organic reaction* types, such as occur in association with structural diseases of the brain due to vascular and degenerative changes, neoplasms, infections, intoxications and deficiency states—*these reactions are predominated by intellectual disturbances; (2) the affective reaction* type, which consists of hypomania and involutional melancholia; (3) the *schizophrenic reaction* type, which consists of the many bizarre modes of thinking, feeling and acting observed in schizophrenia. The most important reaction type in this discussion is the *psychoneurotic*.

Anxiety This is the central symptom presented by the patient in nearly all neuroses and psychoneuroses Anxiety may be defined as one of the clinically important major emotions recognized introspectively as an unpleasant feeling, accompanied by fear without any, or without adequate, cause It is manifested objectively by abnormal changes in the neuromuscular and secretory functions which are emotional expressions All psychoneurotic symptoms are derived from anxiety arising in the conscious or unconscious parts of the personality These symptom complexes include either definite anxiety or conversions and substitutions for anxiety reflected in *disturbances in the physiologic or emotional spheres*. Anxiety gives rise to hostility which, in turn, generates more anxiety. Indeed, certain patients seem to have the ability to create anxiety in the family and finally in the physician Once this has been done, neither the physician nor the patient may realize that hostility toward each other is the prevailing mode The existence of both anxiety and hostility helps to explain the reasons why the neurotic patient is driven imperatively toward *dominating* everyone, toward complying with others but at the same time imposing his will on them, toward detachment from people but at the same time toward a craving for their affection These conflicts may be the dynamic center of the neuroses and the *physician-patient relationship. They are often the bases for* iatric disorders

Hormones. The *hormones* of the *endocrine glands* are not essential to the function of the alimentary tract In the case of the pituitary it is well known that hypophysectomy does not cause any well-defined change in digestive functions.

Hyperthyroidism may be associated with gastrointestinal hypermotility causing diarrhea and symptoms resembling those due to an irritable colon. *However*, toxic

The administration of mercury is a cause for chronic diarrhea in certain instances of poisoning by this agent Arsenic likewise may give diarrhea. Lead, on the contrary, causes chronic constipation

Motor disturbances as a result of a psychoneurosis consist of pyloroduodenal irritability, hyperperistalsis, hypertonicity and hypermotility or hypomotility. A duodenal ulcer-like syndrome may alternate with or accompany the irritable colon symptoms in many psychoneurotic persons It is well to be aware that there is a generalized derangement of motility of the alimentary tract in those who have irritable colon syndrome Disturbances in the motor behavior of the small intestine may be the main manifestations in some instances of the irritable colon syndrome. In these disturbances of the small intestine the roentgenologist may report that the barium meal arrives in the colon in from one-half hour to 4 hours after its ingestion. It seems that the main seat of the dysfunction is in the small intestine

The *coexistence of organic gastrointestinal disease and psychoneurotic symptoms* requires evaluation of the degree of each which is present The evaluation of the etiologic relationship between symptoms is often difficult even after extensive investigation. The presence of an organic lesion may not be discovered Likewise it may be impossible to find an adequate psychogenic cause for the presenting symptoms

It is the consensus that the symptoms of digestive, or any other, psychoneuroses and neuroses imply the absence of any primary structural or chemical disease, the existence of a certain constitutional make-up, the occurrence of precipitating or exciting causes, and the formation of symptoms which may originate in the psychic or in the physiologic sphere or in both The symptom may begin synchronously with the action of some exciting cause which may be an injury, an infection, a chemical disturbance, or some emotional stress

Achlorhydria once was thought to occupy a prominent place in the production of chronic diarrhea At times and under conditions which cannot be elaborated, this may be the cause of loose bowel movements It is well to realize that achlorhydria rarely is accompanied by frequent bowel movements

Chronic diarrhea may follow *gastroenterostomy* This type of diarrhea may be attributed to rapid emptying of the stomach, to gastrojejunitis, or to gastrocolic fistula Occasionally a gastrojejunostomy, a gastroileostomy or an entero-enterostomy between widely separated segments of the intestines may cause diarrhea The continuous elimination of dejecta from an ileac stoma is not considered a diarrhea A diarrhea from an ileac stoma is manifested by a greatly increased volume of dejecta Likewise a diarrhea from a colic stoma is manifested by an increased volume of dejecta

In aged individuals and in those who have congenital megacolons, *fecal impaction* may occur, but a channel is left open through the impaction and chronic diarrhea characterized by the frequent passage of small amounts of feces occurs

Similar mechanical conditions may be produced in the colon by diverticulitis, colonic polyps, factitial sigmoiditis and malignant lesions

Sprue Both tropical and nontropical forms are characterized by frequent bowel movements In these disorders the volume of the feces is increased and it contains increased quantities of fat

The Irritable Colon Syndrome. The terms irritable colon and unstable colon are used to embrace all of the manifestations of the colonic neuroses. The disturbances of the *motor activity* of the colon are the commonest. The *mixed neuroses* are next in frequency. The *secretory neuroses* occur the least frequently.

In the irritable colon syndrome there is present a colonic dysfunction in asso-

complaints

be present

[illegible]ng laxatives

and colonic irrigations are poorly tolerated

Allergic State. Allergy and the *allergic reaction* or allergic digestive symptoms may occur in any person who has been endowed through heredity with the allergic state. In such a person the oral ingestion of specific antigens or antigenic substances may induce allergic symptoms. These symptoms are the manifestations of intestinal hyperemia, edema and increased mucus secretion occurring during the allergic manifestations Since allergic manifestations may be localized or generalized through the alimentary tube the symptoms may be localized or generalized digestive manifestations which simulate functional disorders.

The localized symptoms of digestive allergies perhaps occur more frequently in the colon than elsewhere in the alimentary tract. An allergy may contribute to or entirely account for the so-called irritable colon syndrome in an insignificant number of patients who have this disorder. Colonic dysfunction of allergic origin is more often manifested as isolated attacks of diarrhea and abdominal pain than as severe episodes of abdominal pain associated with vomiting and diarrhea and accompanied by systemic symptoms and signs of shock.

In order to attribute gastrointestinal symptoms to allergy, the first diagnostic requirement is the presence of the allergic state. There should be a genealogic history of allergy There should be a history of definite reactions to the eating of certain foods, drinking certain beverages, or taking certain drugs, or a reactivity to certain extraneous substances In the absence of known reactions to such substances, the presence of hay fever or asthma may be confirmatory evidence. In all instances there should be a periodicity of the symptoms like that present in hay fever and asthma The attacks of abdominal pain or diarrhea should be partially or totally relieved by the administration of epinephrine (0 5 ml. of 1 to 1,000 solution) The presence of an eosinophilia during the attack is important diagnostically.

The ability to relieve symptoms of abdominal pain, diarrhea, and mucus discharge by the withdrawal of foods to which patients seem to be sensitive and the subsequent reappearance of symptoms following the ingestion of those foods are diagnostically helpful, but time and repetition of this sort of diagnostic tests are necessary before a definite diagnosis of an intestinal allergy can be made A psychic colonic disorder will often respond well to the withdrawal of certain foods for short intervals

Nonallergic Foods The ingestion of *various foods* by patients who have a gastrointestinal neurosis may be responsible for the aggravation of symptoms and perhaps, less frequently, for their initiation. Roughage is poorly tolerated by the patient who has an unstable digestion If fibrous foods are ingested, they often aggravate the symptoms In susceptible subjects, the taking of ice-cold or hot food and drink may initiate diarrhea and abdominal pain

Laxatives. The continuous use of *laxatives, enemas* and *irrigations of the colon* for the relief of constipation may cause symptoms similar to those of a colonic neurosis In some instances laxatives or enemas have been administered by charlatans for the relief of auto-intoxication, headaches, constipation, abdominal pain and discomfort, and gaseous dyspepsia These symptoms will cease on discontinuation of the cathartics if a colonic neurosis is not present prior to the employment of intestinal irritants In reality, laxatives and enemas do not contribute to the presence of colonic neurosis and they are not important *etiologically. They* act to stimulate the intestines, and a continuous stimulation will serve to annul the normal colonic reflexes for defecation. If a psychoneurosis is not present, the intestinal symptoms immediately cease on the discontinuance of the use of laxatives and enemas

A common cause of loose bowels is the self-prescription and administration [illegible] cathartics. It is well to inquire in regard to prescribed [illegible] history is being taken in an instance of chronic diarrhea.

Man, possessing an alimentary volume midway between these two animals and eating a sufficient amount of food for maintenance, invalidates the general statement concerning the influence of dietary factors on the development of constipation.

The important cause for constipation is *improper training and neglect* in very early childhood When a child is trained to have bowel movements at a specified time or simply is left alone, there will be no constipation In later life if an individual does not have time for bowel movements and to allow the bowels to act normally, the physician cannot be of any help to him

The lack of *adequate facilities* may be given as the reason for the frequent *neglect to move the bowels after fecal matter has entered the rectum and initiated the* desire to defecate Usually this sensation soon passes off although the fecal matter remains in the rectum It is not until a fresh increment of feces further distends the rectum that the desire to defecate recurs. After a time, because of the constant residence of feces in the rectum, the defecation sense may be blunted and finally may disappear entirely. If toilets are not available, patients may be advised to provide themselves with suitable vessels which can be emptied later.

In the minds of many people there is the idea that a weekly cleaning out by a strong purge is beneficial to the body economy. This practice goes back many centuries and will continue for many more centuries, and its detrimental effects have not been proved It may destroy normal bowel habit

Constipation occurs in persons of all ages who do not or are not allowed to leave the act of defecation to normal controls. Constipation produces no other subjective complaint or objective evidence of disease In cases of simple constipation symptoms are rare except in hypersensitive subjects. Constipation as a symptom of organic disease or of fecal impaction is accompanied by various discomforts depending on the nature of the disease or the cause of the impaction

The history of the manner of onset of constipation will often serve to indicate its

digital, endoscopic and roentgenographic examinations of the anus, rectum and colon

Examination On general examination there is no evidence of loss of weight unless anorexia or sitophobia, functional vomiting, or diarrhea is present There are often found (1) cold, moist hands and feet, (2) dry mouth and lips, (3) variable pulse rate, (4) variable blood pressure, (5) tenseness, (6) tender abdomen and (7) hyperactive tendon reflexes.

Diagnosis A consideration of the possible presence of a functional disorder of digestion to account for digestive symptoms is required in most of those who have symptoms of abnormal digestion The findings on roentgenologic and roentgenographic examinations are the most helpful evidence in addition to the presence of a particular type of temperament and the findings on physical examination In cases of chronic diarrhea the following examinations should be executed in the order given here, the results of examination should be negative. (1) feces for ova and parasites (three examinations on successive days of liquid stools obtained by the administration of 1 ounce of epsom salts to the fasting patient); (2) proctosigmoidoscopic examination; (3) roentgenographic examinations of the stomach, colon and also occasionally the small intestines, (4) composition of the gastric contents (presence of hydrochloric acid); (5) basal metabolic determinations if the presence of hyperthyroidism is suspected, and (6) examination of the blood and urine for evidences of poisoning by certain chemicals such as arsenic and mercury and the presence or absence of leukocytosis and anemia.

In many instances a period of observation is required before a diagnosis can be made

In various places in the medical literature statements will be found that the irritable colon syndrome, including both diarrhea and constipation, is due to the tensions of present-day civilization There are no data to prove that psychic diarrheas and constipation are any more prevalent in modern civilized men and women than they were or are in savages. During the seasons of fresh berries and other fruits most savages have diarrhea When food supplies are scarce, the savages probably are constipated. So far as psychic tension is concerned, the savage, racked by fear of his enemies, torn between the exigencies of strife for his personal existence and the signs and implications of the presence of demons, spirits and gods ready to bring disaster on him, had and has more to be tense about than the present-day civilized men and women.

The shape of the formed stools is frequently displeasing to the patient who has irritable colon The passage of small, hard pellets or scybala may precede or follow an episode of abdominal discomfort Often there are present diarrhea or constipation

Diarrhea. The *history* will often separate a chronic diarrhea due to organic disease from one due to irritable colon In a patient who has organic disease the symptoms will have a definite onset. Often there will be, or will have been, present fever, bloody dysentery, loss of weight, and symptoms which disturb sleep The history in a diarrhea of psychogenic origin will reveal a constancy of symptoms dating indefinitely. There will be no disturbance of sleep from the diarrhea and no loss of weight without the presence of sitophobia Rectal bleeding will be absent unless there is an anal fissure or hemorrhoids.

Mucous colitis is the clinical manifestation of a functional colonic derangement characterized by the discharge of excessive quantities of mucus in the stools in the absence of demonstrable colonic disease

Constipation. Constipation may be defined as an abnormal retention of fecal matter in the intestinal canal or an undue delay in the discharge of excreta from the rectum. Constipation may be a manifestation of the irritable colon syndrome In this syndrome there may be alternating constipation and diarrhea However, there are a great number of stable and stoic individuals who are constipated from causes not necessarily a part of the etiology of this syndrome Some of these causes are made apparent by the following discussion

The causes of constipation are (1) The passage of the food residue and excreta along the colon is abnormally slow (2) The food residue reaches the rectum without delay but defecation is inefficient or difficult The natural *posture for defecation* is the squatting position, with the thighs flexed upon the abdomen In this posture the *capacity of the abdominal cavity is reduced and intra-abdominal* pressure increased, thus aiding the expulsion of the fecal mass The modern toilet seat in many instances is too high Unless the toilet seat is low enough that the feet may rest firmly on the floor and some flexion of the thighs is possible, the accessory muscles which aid in defecation normally have little opportunity to fulfill their function Four muscular structures responsible for the expulsion of the fecal mass are the muscles of the abdominal wall, the diaphragm, the levator ani muscles and the smooth muscle of the intestinal wall, and these should be aided by posture during the act of defecation

If the *upright position of man,* as has been claimed, causes constipation, it is because there is an increase in the distance that the intestines must raise the intestinal chyme against gravity Measurements of this distance are comparable in man and the quadrupeds Likewise it is erroneous to assume that there is lack of support of the intestines of man while in the upright position The ruminant quadrupeds have relatively a much longer alimentary tract, they eat a much greater quantity of food, carry it for longer periods and have no more support of the intestines than does man

The *colon of man* is midway between the size of the colon in the herbivora and the carnivora The herbivora are not constipated. The carnivora may be constipated

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category of disorders may be mentioned genetic dwarfism and gigantism, certain instances of hirsutism, obesity, mongolism, Laurence-Moon-Biedl syndrome and mental retardation of children.

The endocrine glands are so intimately associated with the normal psychic, psychosomatic and somatic constitutions and behavior of the normal person that aberrations in their function permit of wide interpretations. It is for this reason that the literature on endocrinopathies is extensive and often difficult to evaluate. The physician has to be as careful as it is possible to be in the selection of a consultant to help in the diagnosis of the patients who may have an endocrine disorder.

THE PANCREAS

The pancreas lies beneath the stomach and transverse colon, stretching across from the duodenum on the right of the spinal column to the spleen on the left Its body lies over the first and second lumbar vertebrae, its lower edge about 2 inches (5.1 cm) above the umbilicus. Normally the pancreas is not palpable.

The pancreas secretes an external secretion referred to as pancreatic juice or the exocrine secretion It also secretes an internal secretion, insulin. Both the external and the internal secretions are active because of their hormonal content The exocrine secretion passes through the pancreatic ducts into the duodenum and it is concerned with intestinal digestion It contains the digestive enzymes amylopsin, trypsin, steapsin (lipase) and rennin The internal secretion of the pancreas, insulin, is concerned with the control of carbohydrate metabolism

Many diseases of the pancreas are expressed as acute, subacute or chronic localized conditions limited to the pancreas without disturbances of either the exocrine or the endocrine functions These localized diseases at any time may cause disturbances in one or the other or both of the secretory functions of the pancreas Finally a localized disease may extend to involve the pancreas sufficiently to cause a combined disturbance of both the exocrine and the endocrine functions of the organ

The diseases of the pancreas which interfere with the production of the pancreatic juice and its delivery to the intestines give rise to manifestations referable to the digestive system The incidence of these diseases is rare indeed in comparison with the incidence of the diseases due to the interference with its endocrine function, the production of insulin, namely, diabetes mellitus and hyperinsulinism

EXOCRINE DISORDERS OF THE PANCREAS
(Pancreatic Insufficiency)

There are no known examples of disease due to an overproduction of the exocrine secretion of the pancreas.

Deprivation of the Exocrine Secretion (Pancreatic Insufficiency) Deprivation of the pancreatic juice is followed by bulky stools, light in color, soft and watery, passed one to three times daily The total weight of these stools is increased three times normal The increase in weight is due to the increased excretion of fats and proteins Normally 5 to 6 gm of fat are lost in the stools from a 100 gm. daily intake whereas 35 to 45 gm are lost in the feces on deprivation of the pancreatic juice

Normally about 10 gm of protein are lost from a 100 gm. intake. On deprivation of pancreatic juice 25 to 50 gm of protein are lost in the feces

The digestion and absorption of carbohydrates proceed normally when there is deprivation of pancreatic juice

Pancreatic insufficiency occurs when there is injury, destruction or abolition of sufficient amounts of pancreatic tissue to prevent it from secretion of a sufficient amount of pancreatic juice or pancreatic digestive hormones to initiate and complete intestinal digestion. When this is present the symptoms of deprivation of pancreatic

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DISEASES OF THE ENDOCRINE SYSTEM

The term endocrine gland refers to a ductless gland which delivers its secretions directly into the blood stream The secretory products of endocrine glands are variously termed internal secretions, hormones and sometimes autacoids The most appropriate name for the active principles secreted by endocrine glands is hormones. A hormone is the substance carried to the different parts of the body which acts for the good of the organism It is realized that the intracellular hormones are of a separate class from those of the endocrine glands Likewise, the vitamins are hormones derived from plant and animal sources

An endocrine gland may consist of secreting cells, or it may have cell types for an endocrine secretion and another type of cell for the secretion of an exocrine substance Those glands which contain elements for the secretion of an exocrine substance also have a system of ducts or channels for delivery of secretions to the outside The pancreas is an example of the latter type of gland

The process of glandular secretion may range from the separation of a specific substance of the blood to the elaboration of a new specific chemical compound or even the formation of cells as in the case of the formation of ova or spermatozoa

Hormones are numerous and complex, and characteristically their presence initiates very complex chemical actions or enables them to proceed at normal body temperatures They are therefore catalysts in their own rights or they may utilize other catalysts for their activation In the extremes of body temperatures hormones may be inactivated or destroyed

It is known that there are other mechanisms for hormone inactivation Certain trophic hormones seem to be inactivated by their respective target glands For example, thyroid tissue inactivates thyrotropin (lymphoid tissue may act in a similar manner), gonadal tissue inactivates gonadotropin and the liver too can and probably does inactivate gonadotropin.

The mechanism for activation of hormones is buried if possible in more obscurity than that of inactivation

The hormones have not been accorded a regular system of terminology The hormones with known chemical structure are either small molecular weight amines, steroids, or proteins The steroids are secreted by the testes, ovaries and adrenal cortices These structures have their origin from the celomic mesothelium The protein hormones are secreted by the anterior pituitary, thyroid, parathyroid and pancreas These glands originate from the alimentary tract and are therefore of epithelial derivation The adrenal medulla and the neurohypophysis arise from the nervous system and they secrete hormones of a small molecular weight and of the structure of the amines These amines and the steroids are remarkably similar in chemical structure

The clinical manifestations of endocrine disease are observed, not in the gland involved but in the structures susceptible to its hormones. Special studies are required in order to demonstrate that the gland in question is performing its allotted tasks There are many patients who are regarded as having an endocrinopathy by certain endocrinologists who tend to overestimate the diagnostic reliability of the tests employed. Among the disorders so diagnosed are the syndromes of pseudohypoparathyroidism, pseudodiabetes insipidus, pseudo-Addison's disease and that all-inclusive syndrome of hypometabolism The disorders which have heredity as their etiology may be the most difficult to differentiate from endocrinopathies. In this

Acute Pancreatitis. Acute pancreatitis is a rare but a serious and often fatal disease, particularly when there is hemorrhage and necrosis in the pancreas

The acute pancreatitis which may accompany infectious diseases is usually not serious and it is rarely recognized Likewise the pancreatitis which may be diagnosed by the surgeon as an enlarged, indurated head of the pancreas is not a serious disease if the surgeon is able to treat the accompanying biliary disease adequately.

ORIGINS There are three theories to explain the occurrence of acute pancreatitis: (1) the theory of infection, (2) the theory of the common channel (Opie) and (3) the theory of obstruction of the small pancreatic ducts.

Theory of Infection Bacteria present in the bile regurgitated into the pancreas are said to activate the pancreatic enzymes, which cause the initial autolysis of tissue. In infectious parotitis, typhoid fever and scarlet fever bacterial invasion of the pancreas by way of the blood stream or of infection through the lymphatic channels has etiologic significance. Acute pancreatitis occurring in association with such an acute infectious disease is mild and tends to disappear without any serious consequence.

Theory of a Common Channel (Opie) A common channel is formed by the confluence of the common bile duct and the pancreatic duct at a point ahead of their entrance into the duodenum. Such a confluence of these ducts is frequent enough to be considered a normal anatomic arrangement. Bile usually does not enter the pancreatic duct because the secretory pressure of the pancreatic juice is greater than that of the bile Bile, therefore, can enter the pancreas only when there is some sort of obstruction at the ampulla which obstructs the flow of bile into the gut and thus forces the bile into the pancreatic duct and the pancreas When this occurs, activation of pancreatic enzymes either in the biliary passages or within the pancreas takes place and acute pancreatic necrosis ensues Pancreatic enzymes may be activated in the common ampulla or in the biliary passages and then may pass into the pancreatic duct. Many observers have produced acute pancreatitis in experimental animals by injecting bile into the pancreatic ducts

Obstruction of the Small Pancreatic Ducts. Rich and Duff suggested that an obstruction to the small pancreatic ducts, and thus an obstruction to the outflow of pancreatic juice, resulting from pancreatic lithiasis, gallstones, stricture, edema and tumor accounts for some cases of acute pancreatitis.

PATHOLOGY The pathologist usually describes four types of acute pancreatitis, namely, edematous, hemorrhagic, acute pancreatic necrosis, and suppurative.

In edematous types of pancreatitis the inflammation is of long duration The pancreas is enlarged and hardened On section the inflammation is the most manifest in the interstitial tissues This is the usual form of pancreatitis which accompanies cholecystic disease A severer form of inflammation occurs when there is some obstruction of the pancreatic ducts In these inflammations, if some of the smaller ducts rupture, there is necrosis in surrounding tissues Necrosis of the pancreas follows the escape of activated pancreatic enzymes Activated pancreatic enzymes will cause an acute pancreatic necrosis in the absence of rupture of the pancreatic ducts. If there is an escape of infected pancreatic juice, *hemorrhage* may occur, to be followed by suppuration *Suppuration,* however, can occur in the absence of hemorrhage and hemorrhage can occur without suppuration In severe infections and in suppurative pancreatitis, pancreatic abscess may be present

The term fat necrosis is applied to the white opaque areas commonly seen on the surface of the pancreas, the mesentery, omentum, and parietal and visceral peritoneum. In severe pancreatitis the pancreas is large, soft and friable, and dark Hemorrhage or hemorrhagic phenomena may be either present or absent

SYMPTOMS AND FORMS OF ACUTE PANCREATITIS Acute pancreatitis occurs in persons in all decades of life The usual form, the *edematous pancreatitis* occurs most commonly in middle-aged women who have gallstones More than one half these patients are less than 50 years of age This form of the disease is benign, and usually is discovered by the surgeon at the time of surgical operations for gallstones

These patients give histories characteristic of the cholecystic disease which they

juice ensue. The localized diseases of the pancreas which may become diffuse pancreatic disease are the commoner causes of pancreatic insufficiency.

Localized Diseases of the Pancreas. The localized diseases of the pancreas which may be manifested as such or which may extend to cause aberration in its exocrine or endocrine functions are: the prenatal influences, those termed acute and chronic pancreatitis, the specific infections and those of less well-described etiologies.

Diseases of the Pancreas Due to Prenatal Influences. In embryos 3 to 4 mm in length there are two outpocketings from the primitive gut One of these, the dorsal pancreas, is cephalad of the level of the hepatic diverticulum. The other, the ventral pancreas, appears ventrally between the gut and the hepatic diverticulum. Unequal growth of the gut shifts the bile duct dorsad and brings the ventral pancreas into the dorsal mesentery. During the seventh week the dorsal pancreas and the ventral pancreas come together The short ventral duct fuses with the dorsal, and thereafter the long distal duct of the dorsal pancreas plus the entire ventral duct serves as the chief drainage for the external secretion The common outlet for the bile into the duodenum and the pancreatic ducts is but a retention of these primitive relations The proximal segments of the dorsal duct serve as the accessory pancreatic duct.

Accessory Pancreas. The commonest of all the *pancreatic anomalies* due to prenatal influences is *accessory pancreas* Many of the pancreatic rests in the abdomen or in the walls of the adult intestines are associated with the omentum, spleen and stomach. These widely distributed accessory pancreases are but displaced parts of the original primordia An accessory pancreas situated in the stomach or the duodenum may cause symptoms suggestive of gastritis, peptic ulcer, cholecystitis, or pyloric obstruction

Heterotopic pancreatic tissue situated in duodenal diverticula either in the pouch itself or in the duodenum adjacent to a diverticulum may produce intestinal obstruction. These aberrant bits of tissue in the submucosa along the digestive tube may originate intestinal obstruction, ulceration and hemorrhages

The pancreatic anomalies, aside from accessory pancreas, are annular pancreas, pancreatic ducts arising directly from the duodenum, absence of that part of the gland which arises from the dorsal primordium, failure of union between the dorsal and the ventral pancreas, and completely independent ducts.

Annular Pancreas Annular pancreas is characterized by a band or ring of pancreatic tissue which envelops the second portion of the duodenum, the bile duct and the portal vein

In an infant roentgenographic evidence of partial obstruction of the second *portion of the duodenum in the presence of jaundice is suggestive* of annular pancreas On rare occasions annular pancreas may be present without symptoms until adulthood and then be the cause of intestinal obstruction. Annular pancreas causing constriction and obstruction of the duodenum requires surgical treatment

Cystic Fibrosis of the Pancreas. Cystic fibrosis of the pancreas may occur among siblings, twins and more distant relatives. It is a recessive hereditary trait The lesions in the fetal pancreas appear in late intrauterine life and seem to result from an abnormality of the acinar secretion in the pancreas However, comparable disturbances are present in the liver, gallbladder, intestine, lungs, and possibly in the salivary glands. Intestinal obstruction and failure of pancreatic function is often associated with pancreatic fibrosis and secondary changes in the meconium. This intestinal obstruction may be complicated by volvulus or congenital peritoneal adhesions. There is evidence that the pulmonary lesion begins after birth and is primarily the result of *nutritional deficiency.*

Pathologically cystic fibrosis of the pancreas is characterized by obstruction of the ducts of the pancreas, the salivary glands and the trachea and bronchi, with resulting secondary changes

Cystic fibrosis of the pancreas is manifested by the presence of steatorrhea, dwarfism and chronic respiratory infections

glucose formed by the action of 100 ml of serum on starch) is normally 70 to 200 mg, but is increased in 8 of every 10 who have acute hemorrhagic pancreatitis. The intensity of the serum amylase values bears no relation to the severity of the disease. It is related to the acuteness or intensity of the disease, being higher during and immediately following the damage. The serum lipase also is increased.

The urine may contain albumin. Glycosuria, indicating transient as well as permanent diabetes, occurs in fewer than 1 of every 10 patients. When present it indicates severe damage of the pancreas and is most commonly observed in those who have suppurative lesions All patients with glycosuria have an associated hyperglycemia

Roentgenologic studies (scout (preliminary survey) films or simple roentgenograms of the abdomen) may reveal gallstones, gas in the small intestines, or nothing at all

In some instances there may be a similarity between the clinical syndromes of coronary thrombosis and acute pancreatic necrosis. In these, electrocardiography and serum enzyme determinations are required.

The mortality rate from pancreatic necrosis is around 10 per cent Some surgeons think that mortality rates may be decreased if operation is not performed immediately

One of every 10 who survive an attack of acute pancreatitis becomes diabetic. An even greater number are left with minor disturbances of carbohydrate metabolism An undetermined number of patients who survive an attack of severe acute pancreatitis have sufficient pancreatic atrophy and fibrosis to account for the presence of pancreatogenic steatorrhea

The mobilization of calcium in the regions of fat necrosis is said to be associated with a decrease in the concentration of serum calcium

Acute Pancreatic Necrosis. Acute pancreatic necrosis occurs most frequently in obese men between the ages of 30 and 60 years Cholelithiasis is present in about one half of these patients A history of addiction to alcohol is common The onset frequently follows a heavy meal and an alcoholic debauch

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After an attack of acute pancreatitis diffuse suppurative inflammation or a pancreatic abscess may develop In other instances the inflammation is suppurative from the beginning These beginnings of suppuration of the pancreas are lymph-borne or hematogenous infections, extensions of infection from an adjacent organ.

The symptoms of suppurative disease of the pancreas are less intense than those of acute pancreatic necrosis There is a daily intermittent type of fever, and often there are chills and pain in the left upper part of the abdomen extending around to the left scapular region There may be symptoms of subdiaphragmatic abscess on the left side from rupture of a pancreatic abscess. Pus may pass down toward the left side of the pelvis or it may rupture into the lesser peritoneal sac or into the general peritoneal cavity Generalized peritonitis eventually may ensue.

On examination there is tenderness in the left upper portion of the abdomen. Rarely a mass may be palpated

Diagnosis often is not possible. Tests of serum enzyme are of no value diagnostically unless the enzyme content is decreased below normal limits. If suppurative inflammation of the pancreas is suspected, operation should not be delayed

Pseudocysts. Pseudocysts of the pancreas may follow an attack of hemorrhagic necrosis of the pancreas or suppuration of the pancreas

Diagnosis of Acute Pancreatitis. Often a presumptive diagnosis can be made

usually have In the more severe and acute forms of the disease the symptoms are the same as those of *acute pancreatic necrosis but less severe.*

On examination there are tenderness and muscle guarding in the epigastrium and left hypochondriac region often extending straight through to the back.

In the early diagnosis determination of *concentration of serum amylase is of no* assistance. The increase in serum amylase in acute transient pancreatitis is of brief duration. If the serum amylase is increased and drops suddenly to normal in conjunction with clinical improvement, edema of the pancreas is more likely the diagnosis than necrosis of the pancreas. Disturbances in carbohydrate metabolism are less common in acute edematous pancreatitis than *in acute hemorrhagic* pancreatitis There may be transient glycosuria, hyperglycemia or hypoglycemia.

Hemorrhagic Pancreatitis (With Hemorrhage and Necrosis). Hemorrhagic pancreatitis (with hemorrhage and necrosis) occurs most commonly in men, who may or may not have gallstone disease More than one half of these patients are more than 70 years of age Alcoholic debauches often precede this form of pancreatitis

There is an abrupt onset of agonizing pain in the epigastrium, often referred around to the back and to the loins The reference of severe pain to the left side of the epigastrium and around or through to the left subscapular region in an obese middle-aged man or woman is very suggestive of acute pancreatitis In some instances signs and symptoms of *pancreatic necrosis cannot be distinguished* from those of biliary colic or perforated peptic ulcer

The pain of acute pancreatitis is severe and steady It rarely is colicky or intermittent like the pains of intestinal obstruction. In more than half the patients the pain originates in the epigastrium In the rest the pain is generalized throughout the abdomen and flanks or occasionally in the chest and shoulders

Vomiting appears promptly after the onset of pain and tends to recur despite an empty stomach A few patients will have diarrhea The occurrence of gross melena is not due to pancreatitis.

On examination the pulse rate is accelerated, the blood pressure may fall, and collapse may ensue The skin is cold and clammy and there *may be cyanosis. In* some of those who have an acute hemorrhagic pancreatitis there appear spots of cyanotic staining and patches of slate blue color over the abdomen, with petechial patches *on the buttocks and a brownish discoloration just below* the ribs posteriorly. These spots have been thought to be pathognomonic of acute pancreatitis Davis called *attention to a mottling of the skin of the limbs*

The epigastrium may appear distended and the lower part of the abdomen flat by contrast Palpation of the abdomen elicits tenderness most marked above the umbilicus and often to the left of the midline. In severe pancreatitis muscle guarding is present, and often there is rigidity above the umbilicus. On auscultation it may be noted that intestinal peristalsis is decreased or temporarily *absent because* of intestinal ileus, which is so frequently present

An abdominal mass, usually firm, fixed and tender, is palpated sometime in the *course of the disease in one third of the patients* Among the patients who have interstitial pancreatitis a mass appears less frequently, but when present it usually is detected in the right upper quadrant About four fifths of patients with suppurative or cystic pancreatitis have abdominal masses which lie predominantly within the left upper quadrant About one third of the hemorrhagic-necrotic group *will have* abdominal masses situated on the right side of the abdomen Cullen's sign, a faint periumbilical ecchymosis, is rarely present

Leukocytosis is common but not invariably present *When it is* present, leukocytes range from 10,000 to 20,000 or more per cubic millimeter of blood

The concentration of serum amylase (results are expressed in milligrams of

The incidence of chronic pancreatitis is greatest in men who are between the ages of 30 and 50 years The disease also occurs in women

Chronic pancreatitis occurs both in a mild and in a severe form The disease is usually not suspected until it is found by the surgeon at the time of operation for disease of the biliary tract. The head of the pancreas is hard, somewhat nodular and usually enlarged so that the surgeon may suspect the presence of malignancy. Walters has expressed the belief that in these cases of suspected malignancy if cholecystenterostomy or cholecystgastrostomy results in a permanent cure, a diagnosis of chronic pancreatitis is justified five years after the operation

In the severe form of the disease there is a progressive and painless obstructive jaundice A change in the character of the stools is often the first symptom. The stools are soft and there are several motions a day. Once symptoms are present, they are the same as those observed in all of the diseases associated with steatorrhea (see Sprue, Chapter 22). Loss of body weight is progressive.

The physical examination is important because of the absence of evidence of disease except for that referable to the jaundice and the gallbladder. A transient glycosuria in which a tolerance test reveals a true diabetic curve may be present The gallbladder may be palpable, and there may be an absence of bile from the intestine on duodenal drainage If these findings are present in a person more than 45 years of age, carcinoma at the head of the pancreas should be first considered Carcinoma at the head of the pancreas cannot be excluded except by surgical exploration.

In those who have mild diabetes or steatorrhea the diagnosis of chronic pancreatitis may be suspected Irrespective of the manifestations the diagnosis is usually made at the time of surgical operation for disease of the biliary tract

Chronic Relapsing Pancreatitis. Chronic relapsing pancreatitis, characterized by recurring attacks of pain in the upper part of the abdomen, sometimes associated with disturbances in function of acinar and islet cells of the pancreas, is accompanied by steatorrhea, diabetes and calcification The disturbances in function are transient and mild at first, but they later may become permanent Comfort has expressed the belief that this disease is common.

The causes are not discoverable In some instances a long history of alcoholism may precede or attend the clinical onset Alcoholic and dietary indiscretions appear to precipitate acute attacks The disease makes its first appearance at ages from 10 to 66 years, with the mean at 38 years Unlike cholecystic disease, it is commoner in men than in women It is without predilection for the obese

The pathologic changes in the pancreas are determined by examination at operation, by microscopic study of surgical specimens, and by examination at necropsy They vary from edema, inflammation, hemorrhagic necrosis and abscess in the acute phase to atrophy, fibrosis, cysts, calcification and stones The pathologic changes tend to persist and progress in the intervals between recurrent clinical manifestations. The essential pathologic process may be either repeated attacks of acute interstitial pancreatitis, or repeated sublethal attacks of so-called acute hemorrhagic pancreatitis, or a combination of the two The cysts are pseudocysts and are regarded as encapsulated regions of hemorrhagic necrosis Stones may cause the pancreatitis in some cases, but the sequence of events is believed to be more commonly the reverse

SYMPTOMS Often there are chills, moderate fever, diarrhea, nausea, emesis, jaundice and constipation The attacks of pain are characteristically severe, steady and prolonged The pain most often gradually increases in severity, reaches a plateau, and then gradually declines Such a cycle may require from 2 to 35 days for completion The intervals between attacks vary from a few hours to years The seizure of pain requires repeated administration of opiates, which do not terminate the attack.

The painful seizure is the most violent manifestation of the disease which may have occurred recently or over a period of years The pain may be cramping, stab-

on the basis of the history and the physical examination. The diagnosis of acute pancreatitis is more certain if there is an increase of serum amylase and often of serum lipase

The presence of glycosuria and hyperglycemia adds further support to the diagnosis. A progressively increasing hyperglycemia is a bad prognostic omen.

Tests of the Exocrine Pancreatic Functions. The tests of pancreatic function are most profitably employed during or immediately after an attack of acute pancreatitis of any form.

The diseases of the pancreas affecting its external secretion, or secondarily the body as a whole, other than those due to insulin deficiency are not easy to diagnose, and for this reason a number of pancreatic functional tests have been devised.

Evidences of failure of pancreatic function may be detected by the presence of undigested meat fibers, increased amount of fat, and an increase (more than 25 per cent) of nitrogen in the feces. The urine may reveal evidences of disturbances of enzyme excretions and the presence of sugar In the acute pancreatic diseases there may be an increase in the concentration of sugar (hyperglycemia), glycosuria, and diminished sugar tolerance and an increase of serum and urine enzymes

Diseases of the pancreas for which functional testing is performed are either inflammatory or neoplastic, and the functional change produced is either pancreatic insufficiency or an obstructive phenomenon. Insufficiency is usually the result of an advanced diffuse lesion, the obstructive mechanism may result from an acute inflammatory process with minimal fibrotic change or from a neoplasm localized in the head of the pancreas Therefore patients who have mild inflammatory disease and whose pancreatic function is not tested shortly after an attack and those who have only moderate chronic functional change may show normal response In advanced pancreatic insufficiency both the duodenal and the serum enzymes will be diminished; in the obstructive processes duodenal enzymes are diminished, but serum enzymes are elevated.

Amylase By far the most significant test for acute pancreatitis is that for amylase and lipase in the urine and serum

Elevation of amylase (normal value, 70 to 200 units) in the serum in acute inflammation of the pancreas and salivary glands is thought to be due to the swollen tissue obstructing the ductal system sufficiently to increase the rate of reabsorption of ferment. In advanced renal disease retention may cause an elevation of amylase in the blood An elevated serum amylase is considered conclusive evidence of pancreatic edema or inflammation The determination of urine amylase is less reliable than that of serum amylase. The amylase is expressed in milligrams of glucose formed by the action of 100 ml. of serum on starch.

Usually in chronic recurrent pancreatitis the level of serum amylase is significantly elevated only during an exacerbation, but in some instances it may remain high during remissions. Extremely low levels may be recorded in far advanced pancreatic disease. An elevated serum amylase occurs in about a third of the patients who have carcinoma of the head of the pancreas and in the majority of those who have ampullary cancer.

Lipase Normal serum lipase expressed in terms of N/20 sodium hydroxide is 1 ml or less. In acute pancreatitis, in carcinoma of the pancreas, in some patients who have duodenal ulcers, and in cirrhosis of the liver, intestinal obstruction, mumps, and chronic alcoholism, increased values may be obtained.

Chronic Pancreatitis. There are two forms of this condition: one designated simply as chronic pancreatitis, the other known as chronic relapsing pancreatitis

Chronic pancreatitis is the commoner form. It often accompanies cholelithiasis, gallbladder disease, duodenal ulcer and, rarely, obstruction to the pancreatic duct by pancreatic or biliary calculi or new growths Judd and associates found pancreatitis at operation in 26 8 per cent of patients who had disease of the gallbladder or bile ducts. Primary disease of the pancreas, such as acute pancreatitis and pancreatic lithiasis, may be followed by chronic fibrosis of the gland. A few patients who have achlorhydria, gastroduodenitis and cirrhosis of the liver may show evidence of chronic pancreatitis. Necropsy on bodies of chronic alcoholics often discloses some degree of fibrosis of the pancreas.

Syphilis of the Pancreas. Syphilis of the pancreas is exceedingly rare except in congenital syphilis

The coexistence of syphilis and diabetes mellitus is not uncommon. However, diabetes mellitus if of syphilitic origin appears synchronously with the manifestations of syphilis and treatment will cause simultaneous disappearance of both syphilitic and diabetic symptoms. Moore has seen but one instance of diabetes due to syphilis.

The diagnosis of syphilis of the pancreas in the majority of instances is made on the basis of studies of material obtained at necropsy

Pancreatic Lithiasis. W. J Mayo expressed the belief, as have many others, that infection in the pancreas and perhaps stones are produced by disease of the biliary tract Like many of the other diseases of the pancreas, pancreatic lithiasis occurs predominantly in men, whereas gallstone disease occurs most commonly in women. The preponderance of pancreatic stones in men may be associated with chronic low-grade alcoholism The mechanism of formation of pancreatic calculi and the time required in the process are not known

As W J. Mayo pointed out, two types of calcium deposits occur within the pancreas, actual calculi lying within the ducts, and calcification within the parenchyma of the gland

The presence of calculi in the main pancreatic duct may produce incomplete obstruction. The secondary changes are not marked though the ducts become dilated and the glandular tissue gradually atrophies and disappears Inflammatory reaction in the parenchyma, secondary to obstruction, may be more acute than in incomplete obstruction of the ducts, and in some instances actually may lead to acute or subacute pancreatic necrosis, abscess and cyst formation Obstruction of the common bile duct and jaundice may occur. Changes in the liver develop in some advanced instances. Cirrhosis of the liver has been observed in association with pancreatic lithiasis, and tuberculosis has been reported in a few cases

Symptoms Pancreatic lithiasis may be without symptoms. If there be a symptom, it is a severe colicky pain simulating that of biliary colic. The pain begins in the epigastrium, passes along the left costal margin, extends to the low thoracic region of the back and to the left scapula In other instances the pain begins slowly, shortly after a meal, and terminates in severe colic associated with profuse perspiration In some cases the ingestion of alcohol seems to have brought on the pain.

Nausea and vomiting may occur in association with the attacks of colic or independently of them Disturbances of intestinal function similar to those of the irritable colon are frequent

When the lithiasis has been of long duration, diabetes mellitus of varying severity is associated in about one third of the cases.

Examination Tenderness with or without muscle guarding in the epigastrium may be present during an attack of colic There may be jaundice and hepatic enlargement, and both steatorrhea and creatorrhea A glucose tolerance test is performed if minimal abnormality of carbohydrate function is present In other cases the disturbance in carbohydrate metabolism is evident from the glycosuria and hyperglycemia

Pancreatic lithiasis associated with pronounced destruction of the pancreatic parenchyma may cause decrease or complete absence of pancreatic enzymes in the duodenum (Snell and Comfort)

Diagnosis The roentgenogram is the only means of establishing the diagnosis of pancreatic stones Treatment is not indicated if the diagnosis is based on the accidental demonstration of stones by roentgenographic examination of a patient who does not present symptoms.

Surgical intervention is usually advisable for patients who suffer from severe attacks of colic, particularly if intermittent obstruction to the pancreatic duct or acute pancreatitis is thought to accompany the attacks of pain

bing, colicky, steady, bright, dull and aching, constant or excruciating. The painful seizures vary considerably not only among patients but also in the individual patient. The tendency toward more frequent attacks with the lapse of time is a common feature of relapsing pancreatitis.

The primary or initial site of pain is in the epigastrium or over the upper part of the abdomen, the lower part of the abdomen, or in the lower thoracic and upper lumbar portions of the back. The pain may extend to the left shoulder.

Painful seizures last from a few hours to 3 weeks. There may be associated: dysphagia, nausea, vomiting, constipation, borborygmi, diarrhea, abdominal distention and abdominal soreness Chills and fever are common. During the acute attacks of pain symptoms of shock may occur if there has been hematemesis Pruritus often accompanies the jaundice

The course of the disease is characterized by recurring acute exacerbations separated by short or long intervals of relative clinical quiescence Diabetes and steatorrhea may be caused by either mild or severe attacks of pancreatitis In other instances sequelae develop as the result of pressure of the enlarged pancreas, from inflammation, abscess or cyst

EXAMINATION On examination evidence of loss of weight, fever, jaundice, shock, tenderness and muscle spasm, epigastric mass, hepatomegaly and splenomegaly may be found Some of the findings persist in the intervals between seizures Laboratory examinations reveal slight anemia, albuminuria, glycosuria, increased concentrations of blood urea, hyperglycemia and abnormal glucose tolerance Elevation of the concentration of serum bilirubin is common The values for serum amylase and lipase may be increased during the painful seizures, but they quickly subside, and as the disease advances, these values may be reduced below normal An increased amount of total fats in the feces may occasionally be present

DIAGNOSIS The diagnosis of chronic relapsing pancreatitis often is made difficult by the presence of associated disease of the biliary tract. Roentgenologic findings and experience in order to be mindful of this disease are helpful The diagnosis may be established by the history and by results of physical examination alone in some instances. Tests of pancreatic function and roentgenologic demonstration of calcification may prove the existence of disease of the pancreas and aid in the diagnosis After pancreatitis is established, its primary nature in the pancreas is suspected by the exclusion of diseases of the liver and biliary tract The diagnosis is more easily made during acute attacks than during remissions

In the differential diagnosis disease of the biliary tract, especially biliary colic, hydronephrosis, subacutely perforated duodenal ulcer, intermittent intestinal obstruction and heart disease can be excluded in most instances by the history and by laboratory tests Carcinoma of the pancreas or of the ampulla of Vater may cause pancreatitis which at first resembles primary chronic pancreatitis, but carcinoma is progressive Nontropical sprue is excluded, especially in the presence of steatorrhea

Tuberculosis of the Pancreas. Tuberculosis of the pancreas is exceedingly uncommon and rarely, if ever, primary The infection may reach the pancreas by the blood stream, through the lymphatics, by way of the pancreatic duct, or by extension from adjacent viscera

The symptoms occur in the late stages of pulmonary tuberculosis and are primarily those of pancreatic insufficiency and epigastric pain of varying intensity. Emaciation is often extreme. The glucose metabolism is disturbed and melanoderma is frequent The melanoderma may resemble the pigmentation seen in Addison's disease.

The clinical diagnosis is usually not made, but pancreatic tuberculosis should be suspected in patients suffering from pulmonary tuberculosis who have pigmentation of the skin, rapid loss of weight, steatorrhea, diabetes and pronounced pain in the upper part of the abdomen.

Diabetes Mellitus (Hypoinsulinism). The term diabetes mellitus designates a disturbance in carbohydrate metabolism in which there are hyperglycemia and glycosuria which presumably are due to pancreatic deficiency However, hyperglycemia and glycosuria do occur in disorders in which there is no primary pancreatic deficiency. These disorders are described under the heading melituria (p. 1063)

The incidence of diabetes, and thus its importance in the production of disabilities, has been emphasized by the results of the survey of the population of Oxford, Massachusetts, by members of the United States Public Health Service Among 3,500 persons there were 70 cases of diabetes However, there are no data which afford even reasonable estimates of the number of diabetic persons in these United States. Attempts to estimate the number of other persons who are susceptible are even more dubious

Diabetes mellitus is often hereditary and familial. The tendency to develop diabetes mellitus is transmitted as a mendelian recessive character In familial incidence of diabetes mellitus there is a tendency for the disease to appear at an earlier age in successive generations

Obesity is present in about three fourths of adult diabetic patients but its relation to the etiology of diabetes is not clear There is no good evidence to indicate that increased consumption of sugar is responsible for the development of the disease though excessive consumption of sugar is often practiced by the obese who are more likely than others to have diabetes

In practice it is observed that any disease which may destroy or reduce the amount of pancreatic tissue sufficiently may be associated with the onset of diabetes mellitus An example of such a disease is hemochromatosis

Other glands of the endocrine system affect carbohydrate metabolism The anterior pituitary maintains an important relationship with the islet cells in the regulation of carbohydrate metabolism Patients who have hypopituitarism (Simmonds' disease) are very sensitive to insulin whereas those who have hyperpituitarism (acromegalics) are insulin-resistant It seems that a small number of persons have diabetes due to excessive amounts of an anterior pituitary hormone In some diabetics who have an insulin-resistant form of the disease, the resistance has been attributed to anterior pituitary hormones

In some diabetics the sex hormones seem to bear etiologic importance. The possible etiologic importance of the sex hormones is suggested by the increased incidence of the disease at puberty (both sexes) and at the menopause Diabetes commencing at the time of the menopause may be improved by the administration of estrogen

Infertility in diabetic women may be remedied by proper control of diabetes Abortion and overdevelopment of the fetus, however, are of frequent occurrence The sugar tolerance of the diabetic woman may be found decreased during the early part of pregnancy During the last trimester of pregnancy the diabetes may become ameliorated.

It seems likely that the glycogenic adrenal steroids are in some way important in the genesis of diabetes mellitus

Thyrotoxicosis or hyperthyroidism increases the severity of diabetes and renders the control of the disease by insulin more difficult However, the disease is not caused by the thyrotoxicosis The relationship of thyrotoxicosis is likely due to the increased food consumption, the increased general rate of metabolism and the increased secretion of adrenal steroids

Infections do not cause diabetes but they intensify the diabetic state probably by the same mechanism whereby the sugar tolerance in nondiabetic patients is decreased during acute infectious processes This intensification of a disease by infection and the greater liability to infection is also observed in the endocrine deficiencies, which may affect the course of diabetes such as Simmonds' disease, Addison's disease, and myxedema. It seems that tertiary syphilis may be a precipitating factor in the onset of symptoms in potential diabetics and in the early appearance of gangrene in mild diabetics

Calcification of the Pancreas. Calcified deposits in the parenchyma of the pancreas are occasionally found in association with pancreatic lithiasis The average age of patients discovered to have pancreatic calcification is 40 years, but the condition has been found in children. The symptoms of diffuse calcification cannot be stated since lithiasis accompanies the parenchymal calcification The clinical diagnosis can be made only on the basis of roentgenologic examination.

The treatment is surgical if the presence of calculi can be proved and if colics occur.

Pancreatic Fistula. A fistulous tract leading from the pancreas to the abdominal wall may drain all or part of the pancreatic juice externally. Drainage of all of the secretion to the exterior gives rise to severe disturbances of nutrition and metabolism Drainage of a part of the secretion to the exterior does not cause nutritional defects unless the loss of pancreatic juice is excessive.

The commonest cause of pancreatic fistulas is drainage of pancreatic cysts by the surgical procedure of marsupialization A few fistulas are caused by penetrating wounds.

In excessive loss of pancreatic juice an acidosis may ensue. This may be compensated for to some extent if there is a loss of [illegible] chloric acid One of the earliest deviations is t [illegible] proteins are not disturbed except in cases of [illegible] from fluid lost by fistula and vomiting produces hyperazotemia The presence of dehydration, acidosis, hypochloremia and azotemia accounts for loss of weight, extreme asthenia, prostration, anorexia, nausea, and vomiting and oliguria Anemia is common.

ENDOCRINE DISORDERS OF THE PANCREAS

Interspersed between the system of ducts lined by alveolar cells which produce the exocrine secretion or the pancreatic juice, throughout the parenchyma of the pancreas are *islets of epithelial cells which elaborate the internal secretion,* insulin

INSULIN The international unit of insulin is the activity contained in 0 04082 mg of the third international standard preparation (1952)

Regular and Crystalline Zinc Insulin There are no significant differences in the action of *highly purified amorphous and crystalline preparations of* insulin, they are interchangeable when rapid action is desired The insulin prepared from zinc-insulin crystals has a potency of from 25 to 26 units per milligram of solid.

The peak effect of single doses of protamine zinc insulin can be *demonstrated in patients who are fed at a constant rate but is not apparent in* those receiving reasonably large doses regularly every 24 hours Once overlapping effects have been established, the active insulin is released at a more or less constant rate

A mixture of regular insulin and protamine zinc insulin is capable of combining rapid and prolonged effects By varying the proportions of the two, it is possible to fit the individual requirement

The reactions to protamine zinc insulin are similar to those encountered after the use of unmodified insulin Their onset, however, is more insidious, and they occur many hours after the injection, that is, late in the evening or in the early morning Headache, nausea and vomiting may occur owing to a hypoglycemic reaction 12 to 24 hours after the injection of the protamine zinc insulin.

Insulin ameliorates the symptoms of diabetes, but the nature of the underlying disturbance and the mechanism by which insulin produces its effects are still unknown

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The endocrine diseases of the pancreas are characterized by either a deficit or an excess production of insulin. Since the amount of available insulin exerts the main controlling influence over the concentration of the blood glucose, hypoinsulinism is manifested by hyperglycemia and hyperinsulinism is manifested by hypoglycemia

diabetes The diabetic patient who has one of these diseases may complain only of symptoms referable to it

Diffuse aches and pains, with or without evidence of peripheral nerve involvement and weakened vesical control and attacks of nocturnal polyuria and diarrhea may occur during the course of diabetes mellitus. In children enuresis is often the first symptom to attract attention. Abdominal pain beginning after the onset of the digestive disturbances is often an indication of impending coma. Anorexia is more commonly observed in children than is an increased appetite.

Ocular discomforts may be the subject of the complaint for which the patient seeks aid from the ophthalmologist In many cases the finding of early diabetic retinitis aids in the diagnosis

EXAMINATION. On examination most patients who have severe uncontrolled diabetes appear tired and have evidence of recent loss of weight and dehydration The skin may have lost its elasticity, its turgor and subcutaneous fat and may appear dry Examination of the skin of the soles and palms of children may reveal xanthosis.

The eruptive xanthomas secondary to the hypercholesteremia and lipemia of uncontrolled diabetes come and go with the lipemia Eruptive xanthoma occurs in any xanthomatosis in which there is hyperlipemia Furunculosis and pyogenic infections are common findings if the diabetes is not under adequate control.

The diabetic patient is more susceptible to infections than are normal persons For example, even with the use of insulin, findings suggestive of tuberculosis are about three times as common among diabetic persons as among the general population Findings indicative of tuberculosis in the diabetic patient tend to appear suddenly and to progress swiftly There is often a rapid loss of weight

Enlargement of the liver with infiltration with fat is a frequent finding in chronic diabetes, particularly in children It is usually an evidence of poor control of the diabetes.

The incidental finding of gallstones is higher among diabetic patients than among persons in normal health

The presence of cardiovascular disease is a frequent finding on examination of the diabetic patient at a much younger age than in normal persons The high incidence of arteriosclerosis in diabetes may be accompanied by other degenerative changes in the blood vessels in consequence of an abnormal metabolism.

Gangrene may be present in the toes, less frequently in the fingers Commonly the gangrene of the diabetic patient involves the whole foot The arteries of the leg will be found badly sclerosed up to the knee with decreased or impalpable pulses

Hypertension is an important and a frequent concomitant of arteriosclerosis in diabetes Hypertension and arteriosclerosis are both responsible for the observed myocardial changes Coronary heart disease among nondiabetic patients is found several times more frequently in men than in women However, coronary heart disease is present more frequently in diabetic women than in nondiabetic women

The peripheral nerves of the lower extremities are found to be affected more severely than those of the upper extremities, the peroneal nerve being more vulnerable than the tibial, the ulnar than the radial or the median Diabetic neuritis is characterized by weakness and paresthesias. The patient walks with a broad base, with shuffling gait, there is swaying in the Romberg position There may be slight ataxia Muscular power is impaired The tendon reflexes may be absent There may be present impairment of the sense of pain, of temperature, of vibration and of position, and hypalgesia over the feet and ankles.

The commonest ocular findings in diabetes are irregularities of the posterior surface of the cornea, retinal hemorrhages, exudates in the retina, and diabetic retinitis and catarac[illegible]

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The specific gr[illegible]

In some cases the pathologic changes suffice to account for the occurrence of diabetes; in others they do not account satisfactorily for the dysfunction of the islet tissue When pathologic changes are present these are: (1) hyalinization of the islet cells present in about one third of those more than 40 years of age and (2) fibrosis observed in one fourth of the elderly patients. The islet cells in the young diabetic generally appear to be within the limits of normal.

Changes in other endocrine organs may be present in the diabetic. A decrease in the number and size of the eosinophilic cells of the pituitary gland may be present but this finding is not constant At necropsy degenerative changes in the anterior lobe (resulting from hemorrhage) have been observed in cases in which spontaneous amelioration of the diabetic symptoms occurred during life presumably as a result of the pituitary infarction

Arteriosclerosis is found at necropsy in all cases in which there had been diabetes for 5 years or more. Infarcts of the heart, coronary sclerosis, and arteriosclerosis of the aorta are present in a large proportion of the cases Infiltration of glycogen in the kidneys, hepatic cells, and cardiac muscle, and the deposition of lipids in the reticulo-endothelial tissues may be present

The *Kimmelstiel-Wilson syndrome* occurs in mild hypertensive diabetics of middle age This syndrome is characterized by widespread edema, albuminuria, hypertension and failure of renal functional activity There is present a peripheral neuropathy with locomotor sensory disturbances which simulate tabes dorsalis of syphilis There is present a retinitis which combines the characteristics of the diabetic and the advanced glomerulonephritic retinopathies. Congestive heart failure, hypoproteinemia, and hyperazotemia ensue.

In summary, despite the fact that the islet cells in the diabetic pancreas often show little or no detectable histologic changes it would seem that true diabetes mellitus in all cases is due to disease of the islet cells, as a result of which they no longer elaborate a requisite amount of insulin.

SYMPTOMS. In 1 of every 5 who have diabetes it becomes manifest in the first decade of life. In approximately half of all who have the disease the onset occurs between the ages of 40 and 60 years. There is a declining susceptibility thereafter While diabetes affects all races, the Irish and the Hebrews are said to be particularly susceptible to the disease

The symptoms of diabetes may commence during an acute pancreatitis in those who survive the attack Early diabetes may be asymptomatic, the disease being discovered in the course of a routine examination of urine or blood Patients who have well developed diabetes complain of weakness and fatigue, loss of weight, polyphagia, polydipsia and polyuria (the cardinal symptoms)

In elderly patients who have a mild form of diabetes, polyphagia may precede glycosuria by years Polydipsia and polyuria are associated with hyperglycemia and glycosuria. Also polydipsia may be secondary to excessive loss of extracellular fluid or be accentuated by a chronic nephritis

Generalized weakness and easy fatigability may be the only symptoms of the disease. Backache and impotency are frequent complaints and in some patients may constitute the initial symptom or chief concern Polyuria and particularly nocturia may accentuate fatigue by interrupting sleep

Most patients are aware of appreciable loss of weight by the time the diagnosis is established Loss of weight is due to loss of glucose and ketone bodies in the urine, to loss of fluid and mineral resulting in dehydration, and to the increased metabolic rate. In most patients loss of body weight is indicative of the severity of the disease

Infections of the skin, such as furuncles and carbuncles, are frequent complaints Pruritus vulvae occurs in diabetes, but this condition is generally not due to diabetes Infections in the urinary tract are common in diabetes, particularly in association with the glycosuria of uncontrolled diabetes There is a relatively high incidence of pulmonary tuberculosis, cholecystitis and cholelithiasis among patients who have

excess of the capacity to utilize them, and acidosis ensues The serum bicarbonate concentration decreases as base combines with the acid metabolites, and sodium and potassium are excreted in the urine combined with the acid end products Progressive acidosis and dehydration further impair the utilization of insulin and hence aggravate the deficiency

The symptoms of an acidosis consist of progressive weakness, with malaise, headache, and thirst On examination the mucous membranes are dry, the eyes are sunken, the eyeballs decreased in size and soft, and the breath has a sweet odor. Often abdominal pain and muscular cramps due to sodium deficiency may be present As the acidosis progresses, hyperpnea and the Kussmaul type of respiration appear The loss of sodium results in severe dehydration with hemoconcentration As the acidosis and dehydration increase, the pulse becomes rapid and feeble, the temperature subnormal and the blood pressure falls At this point peripheral circulatory collapse and shock quickly ensue At this time leukocytosis is usually present

Acetone is the first of the ketone bodies to appear in the urine, and then acetoacetic acid and beta-hydroxybutyric acid follow In those who have renal impairment, large quantities of acid metabolites may accumulate in the serum, causing a marked reduction in the concentration of the serum bicarbonate without the appearance in the urine of appreciable quantities of acid metabolites

A carbon dioxide-combining power of serum of less than 10 mEq. per liter indicates the presence of severe acidosis, with coma A carbon dioxide-combining power of serum between 10 and 20 mEq. per liter accompanies moderate acidosis

Arteriosclerosis and Atherosclerosis Diabetes mellitus is often associated with excessive arteriosclerosis Arteriosclerosis develops in young diabetic adults who have an inadequately controlled diabetes In addition to the deficiency of the hormone insulin, there is a dietary or nutritional factor, related to fat metabolism, which contributes to the development of arteriosclerosis in these young patients

Postmortem examinations have provided evidence that in young persons who have had diabetes of more than 10 years' duration the lesions of the arteries are of the three common types, namely, calcification and sclerosis of the tunica media of the Monckeberg type, intimal atheromatosis involving the aorta as well as the coronary arteries, and arteriolar sclerosis evident especially in the renal and retinal vessels Roentgenologic examination of the legs of youthful patients who have diabetes often reveals arteriosclerosis

On general physical examination if a youth is found to have arteriosclerosis he [illegible] examined for evidence of diabetes mellitus Often [illegible]
[illegible]
[illegible] About one fourth of all deaths in diabetes not occurring in coma are due to heart disease which is terminated by coronary thrombosis

Gangrene beginning in the toes, or less frequently in the fingers, is a common complication of diabetes mellitus and arteriosclerosis Gangrene may be instituted by mild trauma such as trimming the toenail or by shaving off too closely a corn with a razor blade Infection follows immediately.

Endocrine Pancreatic Function and the Glucose Tolerance Tests. The fasting blood sugar concentration may be normal in the diabetic individual if there is only mild impairment of the functional activity of the islet cells of the pancreas.

When glucose is ingested, it is rapidly absorbed through the stomach and duodenum The blood glucose concentration rises immediately and reaches its maximal concentration, in the normal person, in about 1 hour and it returns to normal concentration in from 2 to 3 hours.

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sugar content despite the fact that the volume of urine is increased. The kidneys in diabetes are often affected. There is an albuminuria. As the renal functional activity decreases there is hyperazotemia and finally renal decompensation and failure

In diabetes the fasting blood sugar may be as low as 130 mg per 100 ml. but is more commonly about 150 mg. In severe diabetes the value for blood sugar may be more than 300 mg In diabetic coma values of 300 to 600 or more mg. per 100 ml are present in some cases. A fasting blood sugar of more than 120 mg. per 100 ml is usually due to diabetes mellitus. In diabetes, normal, low, or high cholesterol values are encountered

There is no correlation between the incidence of acidosis and coma and a high blood lipid value, nor is the degree of the cholesteremia dependent on the severity of the acidosis or on the height of the blood sugar values. In severe diabetes the blood may appear milky, owing to the lipemia, the fat content reaching high values in extreme cases as compared to 0 to 600 mg per 100 ml for the normal.

In mild or moderate degrees of diabetes the basal metabolism is normal. In those whose body weight is within the limits of normal and who have severe diabetes the metabolism frequently is elevated, whereas in patients on reduced fasting diets it usually is reduced below normal

Diagnosis The criteria required for the diagnosis of diabetes mellitus are glycosuria, fasting hyperglycemia (blood glucose concentration of more than 120 mg per 100 ml), and in mild diabetes a diabetic type of glucose tolerance curve

Complications The complications of diabetes may be manifested acutely or chronically In either case the patient may seek medical aid for the complication rather than the disease The acute complications of the disease are mainly ketosis and acidosis

Ketosis (Diabetic Acidosis and Coma). Formerly it was believed that formation of *ketone bodies* was an abnormal metabolic process due to incomplete combustion of fatty acids and that it was necessary to metabolize carbohydrates in order to utilize the ketone bodies completely

Ketone bodies and ketosuria are usually associated with the acidosis of diabetes mellitus Studies carried out by Waters, Fletcher and Mirsky, using a heart-lung preparation, when the amount of glucose and ketone bodies in the blood could be regulated at will, have shown that glucose is not necessary for the metabolism of ketone bodies The fact that insulin can reduce ketosis and still not increase the utilization of ketone bodies in extrahepatic tissue leaves only the possibility that insulin prevents the formation of increased amounts of ketone bodies by the liver

The concept has been brought forth that insulin may be either ketogenic or antiketogenic When insulin is given in such amounts that hypoglycemia results, there is a reduction of the glycogen stores in the liver, since there is a tendency to maintain the glucose level of the blood Concurrent with the low hepatic glycogen there is an increased metabolism of fat by the liver and a resulting ketonemia and ketonuria On the other hand, if insulin is given in amounts sufficient to halt glycogenolysis, there will be an increased carbohydrate utilization by the liver and a resulting decrease in fat oxidation which will reduce the amount of ketone bodies produced. Thus, in man, ketonuria and aglucosuria may be present at the same time, it appears that ketonemia and ketonuria are normal physiologic responses to a lack of carbohydrate and an increased metabolism of fat in the liver

Diabetic acidosis and coma *are the result of accumulation of excess products of intermediary metabolism of protein and fat in conjunction with severe dehydration* and depletion of mineral Immediate causes of acidosis may be inadequate insulin dosage or added insulin requirement during infections, surgical procedures, trauma, vomiting and diarrhea, and thyrotoxicosis

When an inadequate insulin dosage has been administered in the presence of infection, intermediary metabolites of protein and fat combustion are formed in

excess of the capacity to utilize them, and acidosis ensues. The serum bicarbonate concentration decreases as base combines with the acid metabolites, and sodium and potassium are excreted in the urine combined with the acid end products. Progressive acidosis and dehydration further impair the utilization of insulin and hence aggravate the deficiency.

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Glucose tolerance tests consist in measuring the blood sugar level at stated intervals following oral or intravenous administration of a standard dose of glucose.

Concomitant specimens of urine should be analyzed for sugar. Glucose tolerance tests may be carried out by a variety of means. It is advisable to become familiar with one type of test in order to give confidence in the interpretation of results and the factors which tend to modify it

The glucose tolerance test expresses the total disturbances in carbohydrate metabolism without revealing whether the disturbance is due to a failure in hepatic or tissue glycogenesis, inability to maintain a normal blood sugar by glycogen or protein metabolism or an inability of the tissues to utilize glucose.

The glucose tolerance tests commonly used are: (1) the carbohydrate test meal, (2) the standard 1-dose, 3-hour test, (3) the Exton-Rose 2-dose, 1-hour test and (4) the intravenous test.

The carbohydrate test meal is less commonly used

The standard 1-dose, 3-hour test is often modified to extend over only 2 hours. The test is considered negative for diabetes if the blood sugar concentration after the ingestion of glucose returns to normal within 2 hours Under these circumstances the actual height reached by the blood sugar is unimportant. The height of the blood sugar in diabetes usually exceeds 180 mg. of glucose per 100 ml of blood during the test The blood glucose in diabetes remains elevated above normal for more than 2 hours

The urine may contain glucose even though the blood glucose has not exceeded 170 mg. per 100 ml at any time during the test and still the patient not have diabetes In diabetes there is glucose in at least two of the urine specimens

In the Exton-Rose test the blood glucose level in the diabetic patient increases more than 25 mg per 100 ml of blood during the second hour and the blood glucose concentration is more than 160 mg. per 100 ml at the end of the second hour The urine of a diabetic patient usually contains sugar

After 0 5 gm of glucose per kilogram of body weight administered intravenously in a 20 per cent solution to a diabetic patient the blood sugar concentration remains above normal for more than one and one half hours.

The errors of interpretation of any of the glucose tolerance tests are many and variable These may be enumerated as: (1) Failure to perform test on a *fasting* individual. In such an instance there is a glucose concentration which exceeds the upper limits of normal of 120 mg per 100 ml (2) A restriction of carbohydrates in the diet prior to the test dose of carbohydrates will produce an abnormally high hyperglycemia and a glycosuria in a normal individual On the contrary a diet high in carbohydrates prior to the test dose of carbohydrate will decrease the degree and the prolongation of the hyperglycemia F [illegible]
a more marked hyperglycemia when the [illegible]
rich in carbohydrate If there is any dou [illegible]
taining 80 gm of protein and 300 gm of carbohydrate for 3 or 4 days prior to the test (3) When there is a question of the factor [illegible] there is in some the test may be diagnostically helpful in a negative [illegible] the usual hyperglycemia after the test dose of carb [illegible] tion is being tested when there is a suspected failure of intestinal absorption the *intravenous test should be administered* (4) *Endocrine dys*functions other than that of pancreatic failure may cause aberrations in response to the test doses of carbohydrate For example, hyperpituitarism gives a response like that of diabetes, while [illegible] of an increased glucose toler- [illegible] est should be avoided Exer- [illegible] emia is not necessarily due to [illegible] ive glycogenesis in the liver and tissues or a protein disturbance when the glycogen reserve is decreased.

Hypoglycemia in the Infant. The diabetic mother may pass on to her *child* an innate susceptibility to diabetes In addition to this the newborn of the diabetic mother may suffer from attacks of hypoglycemia and require early and frequent feedings or the injection of glucose The weight of the infant, unless the child is excessively small,

does not influence the mortality rate, which is about four times as great among infants of diabetic mothers as among those of nondiabetic mothers

Postoperative Convalescence. Postoperatively the diabetic patient is exposed to the risk of acidosis, necrosis of tissue, hypoglycemia due to overdosage with insulin, and the complications of arteriosclerosis. It is advisable to administer about two thirds of the usual dose of protamine-zinc insulin on the morning of the operation. After operation, crystalline or regular insulin is given every 4 to 6 hours in doses determined by the findings in the urine or preferably by the blood-glucose levels Lesions requiring surgical intervention, as well as the operation itself, increase the patient's insulin requirement.

The principal cause of death in operations on diabetic patients is arteriosclerotic heart disease

Nonpancreatic Melituria and Other Reducing Substances in the Urine. Following the ingestion of a meal there occurs in the urine of normal persons an increase in reducing substances. This *glycuresis* is due to the excretion of small quantities of glucose and unassimilable carbohydrate with its decomposition products

Following the ingestion of abnormally large quantities of cane sugar, glucose or starch, a certain proportion of normal persons show an appreciable glycosuria which is of no clinical significance This form of glycosuria is termed *alimentary glycosuria*

Transient glycosuria may occur in thyrotoxicosis as well as marked anxiety states and after the intravenous administration of glucose

Glucose is found in the urine of 10 to 20 per cent of pregnant women Since diabetes mellitus may first manifest itself during pregnancy, it is essential to check the fasting level of blood sugar in every case of pregnancy glycosuria and to follow the course of the glycosuria after gestation

Glycosuria occurs frequently in patients who have acute nephritis, nephrosis, and nephrosclerosis In the late stages of diabetes and nephrosclerosis, relatively high values for blood sugar may appear

During lactation the urine may contain appreciable quantities of *lactose*. *Galactose* may be present in the urine after the ingestion of galactose Occasionally it is observed in nursing babies who have gastrointestinal dysfunction

Fructosuria is most likely to be detected following the ingestion of large quantities of this sugar, particularly in the presence of hepatic insufficiency Essential fructosuria is a rare inborn error of metabolism associated with constant levulosuria and without apparent disturbance in the metabolism of other carbohydrates Fructose may appear in the urine in conjunction with glucose in diabetes mellitus.

Pentosuria most commonly occurs as a transient melituria following the ingestion of large quantities of plums, prunes, cherries and grapes In rare instances essential pentosuria occurs as an inborn error of metabolism which appears to be hereditary in nature It is of no significance

The diagnosis of the type of melituria, that is, the specific sugar which is being excreted, requires the use of complex and expensive laboratory procedures. In the presence of a normal blood sugar concentration with history suggestive of some one of the foregoing conditions having been extant, melituria due to a sugar other than glucose can be fairly safely diagnosed provided undue retention of the urine in the bladder is excluded and insulin had not been administered prior to the urine test.

Renal Disease and Glycosuria. In contrast to the innocent renal glycosuria there are glycosurias due to renal disease In various types of renal disease the tubular capacity to reabsorb glucose may be lowered as it is in benign renal glycosuria Usually, however, glomerular filtration is decreased proportionately, and hence there is no glycosuria If the tubules are principally affected, glycosuria will appear The elderly diabetic patient will manifest a lesser degree of glycosuria at a given blood sugar concentration than the younger patient This is because of the

greater frequency of nephrosclerosis in the aged. *Renal factors* must thus be tak into account in evaluating the significance of glycosuria in a given patient

Renal Diabetes (Diabetes Innocens). The renal threshold for glucose in th normal individual varies from 150 to 180 mg. per 100 ml. of blood. The averag value is 160 mg per 100 ml. of blood. In diabetes mellitus the threshold may b raised and may reach 200 or more mg per 100 ml. of blood. In renal glycosur glucose may appear in the urine in the presence of a blood glucose concentratio which is within the range of the normal.

Glycosuria occurring when the blood glucose is within the range of the norm has been termed renal diabetes, diabetes innocens, or benign diabetes, in which th level of blood sugar is normal in the fasting patient In some patients the value fo blood sugar rises above the renal threshold for glucose but the glucose is quickl excreted in the urine while in others the glucose is excreted immediately even a normal blood glucose concentrations.

Renal glycosuria generally is regarded as a rare disorder Among young adul examined for induction into the army, however, Blotner and Hyde found 33 in stances of renal glycosuria among 367 who had glycosuria, an incidence of 9 pe cent

Renal glycosuria may occur at any age There is a high incidence of diabetes i the families of patients manifesting renal glycosuria, but no case in which this benig condition progressed to diabetes has been reported

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The glycosuria following the intravenous administration of glycose is not be to considered either a renal glycosuria or diabetes mellitus. It is due to the norma renal threshold for glucose having been exceeded as the result of the administration of glucose

The prognosis of renal glycosuria is good, with normal life expectancy The amount of sugar lost in the urine is relatively slight and hence does not induce any evidence of malnutrition.

Reducing Substances in the Urine. The copper-bearing solutions used in the analysis of urine for sugars may be reduced by substances in the urine other than sugars Among the many substances which may cause this false positive reaction on analysis of the urine may be mentioned, excessive amounts of uric acid, nucleoprotein and conjugate glycuronates which may be formed after the administration of camphor, chloral hydrate, salicylates, pyramidon (aminopyrine) and sometimes morphine Reducing substances may appear in the urine after the ingestion of various poisons and particularly in poisoning by the phenols The administration of chloroform may produce reducing substances in the urine.

In practice, reducing substances in large quantities in the urine of a patient not receiving medication and who has not been poisoned may be considered to be sugar Every patient who has a melituria is to be considered a diabetic until proved not to have diabetes

Hyperinsulinism. Hyperinsulinism implies an excessive secretion of insulin by the pancreas resulting in hypoglycemia The common example of hyperinsulinism

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with symptoms of varying intensity. There are feelings of hunger, apathy or confusion The patient may be irritable and hysterical and quickly lapse into unconsciousness

... is seen in the early stages of the reaction he appears pale and weak

with moist skin and trembling muscles The pulse is full and rapid and the blood pressure is often increased There is a hypoglycemia. The response to the administration of glucose is rapid.

Insulin shock, when unconsciousness is present, is differentiated clinically from diabetic coma by the moist, pale skin, normal consistency of the eyeballs by touch, muscle tremors, normal respirations, full pulse and hypoglycemia The most important diagnostic procedure may be a search of the personal effects of the patient for *a card indicating that the patient is a diabetic*

Analysis of the urine may not be helpful for the urine may or may not contain glucose.

Spontaneous Hypoglycemia (*Hyperinsulinism*) Spontaneous hypoglycemia occurs in association with islet cell adenomas, adenocarcinomas and in functional or organic disease which may be caused by disturbances in the adrenal glands, liver, pituitary, thyroid, thymus, muscular system or nervous system, as well as by exercise, undernutrition, lactation and other conditions in addition to altered production of insulin.

Hypoglycemia-like symptoms associated with neurosis occur relatively frequently In these neurotic patients there is the emotional instability and a psychoneurosis. The fasting blood sugar concentration is within normal limits. The attacks, which occur usually before meals, can be relieved by remedies which have no pharmacologic potency. The neurotic patient does not have attacks during the night unless the patient knows that such are supposed to occur

Adenomas of the islet cells (islets of Langerhans) are rare. There are only a few proved cases of these tumors Even if these tumors are present, it is averred that only 2 of every 10 persons who have nesidioblastomas (islet cell tumors) have symptoms When present, these tumors are numerous and widely dispersed through the pancreas The mass of islet cell adenomas in an affected pancreas may exceed the mass of islet cells in the normal pancreas Likewise the insulin concentration in these abnormal cells is from 4 to 40 times the amount of insulin per unit of weight of normal pancreatic tissue Adenomas have no sex or age preferences The malignant islet adenomas lack encapsulation and have microscopic evidence of invasion, the presence of tumor cells in the blood vessels, and metastasis

Malignant insulinomas often occur in persons from 15 to 20 years of age The associated hypoglycemia tends to be severe and difficult of management The attacks occur frequently, can be precipitated easily by withholding food, and tend to increase in intensity.

The malignant character of the islet cell tumors which have been diagnosed as malignant on the basis of their histologic appearance is not always borne out by the duration of the life of the patient. In a few instances these patients have lived for 10 years after removal of a large part of the pancreas without recurrence of symptoms

In those who have adenomas or adenocarcinomas of the islet cells of the pancreas there are pathologic changes in the brain consisting of capillary dilatation, scattered small hemorrhages, perivascular infiltration of lymphocytes, atrophy of the cortex with degeneration of the ganglion cells, and swelling of the glia and axis cylinders

SYMPTOMS Tumors of the islets of Langerhans may exist without any clinical indication that they are present When these islet cell adenomas make their presence known, there are hyperinsulinism and a characteristic syndrome of hypoglycemia, very much the same as that produced by an overdose of insulin or the reaction from epinephrine

Characteristically the attacks appear in the early morning hours before breakfast, or during the day, after some undue physical exertion, or after postponement of a meal The patient volunteers the information that eating prevents the attacks and affords immediate relief from symptoms The spontaneous hypoglycemic syndrome begins with an acute attack of exhaustion and fatigue which may increase rapidly in severity until there is loss of consciousness, or until there are convulsions, or both

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Unless there are special symptoms, such as those occurring in some instances of islet cell adenomas, the clinician is often unaware of the presence of these benign pancreatic tumors until the symptoms from pressure arise or he finds a tumor on physical examination.

Benign Tumors. Benign tumors of the pancreas usually are discovered at necropsy without having produced any known symptoms. These tumors are adenomas (islet cell), fibroadenomas, fibromas, lipomas, myxomas, chondromas, and benign cysts.

The cystic tumors of the pancreas comprise a group of uncertain genealogy as to whether they arose as cysts or whether they are true tumors with secondary cystic degeneration

Pancreatic cysts may present themselves as symptomless tumors in the mid or left epigastric regions or as tumors in this situation producing pressure symptoms These cysts are important sources for pancreatic fistulas after they have been marsupialized by the surgeon.

The *large cystic tumors* which compress adjacent structures will eventuate in death unless they are removed There is always the possibility, too, that malignant change may occur or has occurred Any tumor of the pancreas is suspected as being malignant until definite information to the contrary is available

Benign pancreatic cysts often develop after trauma, obstruction of pancreatic ducts, or pancreatitis Pratt estimated that precedent trauma is the basic etiologic agent in one third of all pseudocysts. Obstruction of the pancreatic ducts by calculi, gallstones, swollen lymph nodes and *Ascaris lumbricoides* may be a causative factor.

An acute pancreatitis in association with hemorrhage and necrosis is believed to be the basic factor in the production of many pseudocysts and degeneration cysts, or hemorrhagic cysts In 47 cases of pancreatic cyst, Judd was able to identify an associated pancreatitis in 4 Pancreatitis with contraction of fibrous tissue may be capable of producing obstruction of ducts and thus causing the ensuing dilatation—a mechanism operative in cystic fibrosis of the pancreas present at birth

The factor of cholecystitis in the production of cysts is, like many of the other supposed etiologic factors, difficult to elaborate Judd, Mattson and Mahorner found that only 16 of 47 of their patients gave any evidence of cholecystitis and that 13 of these 16 had only gallstones

The proliferative cysts are adenomatous tumors which have an inherent tendency to form a cyst or which for some reason undergo degeneration and liquefaction

Congenital cysts of the pancreas may be present in association with polycystic disease of the kidneys and liver In rare instances an isolated dermoid cyst may be found

Pathologists classify pancreatic cysts as (1) proliferative cysts (cystadenomas), (2) retention cysts, (3) cystic fibrosis of the pancreas, (4) congenital cysts, (5) degeneration cysts and (6) parasitic cysts and pseudocysts.

Cysts in the pancreas vary in size and number They have smooth surfaces and seem, at times, to be easily ruptured Their contents are as variable as the origins of cysts themselves Pancreatic cysts often remain symptomless for a long time before the patient seeks help Some of the patients reported by Judd had had pancreatic cysts more than 20 years

The symptoms may commence with an awareness of slight discomfort and fullness in the upper part of the abdomen for a long time before there is pain. Nausea, vomiting, and constipation develop, and loss of weight ensues The patient is aware that the pain increases in severity as the girth of the abdomen increases.

As the cyst enlarges there may develop jaundice, ascites, edema of the lower extremities, and intestinal or ureteral obstruction Dyspnea may be present when the cyst is large Destruction and compression of the surrounding pancreatic tissue may

The many symptoms may be enumerated as sweating, flushing, pallor, chilliness. trembling, dizziness, weakness, and palpitation of the heart. During the attack often there are hunger, nausea and epigastric pain The abdominal pain may mimic, and is occasionally thought to be, the pain of peptic ulcer.

In some the central nervous system is profoundly affected. The manifestations are headache, restlessness, dysarthria, diplopia, tonic or clonic muscle spasms, convulsions, hyperreflexia, bilateral plantar extension, and, in extreme instances, coma and death The psychiatric components may comprise emotional instability, fear, disorientation, irritability, automatic behavior, negativism, delirium, mania, amnesia and stupor or unconsciousness. Severe attacks of disturbance of the central nervous system may leave residual headache and spasticity; occasionally palsy or an abnormal mental state will persist for a period after subsidence of an attack Generally the changes due to the nervous system are reversible on treatment.

Examination Physical examination, except during the attack, reveals no abnormality referable to hyperinsulinism During an attack the concentration of blood sugar is usually less than 50 mg per 100 ml and frequently is less than 30 mg (Wilder) The value for fasting blood sugar in these patients often is normal but tends to be decreased

The application of the usual tests of hepatic function will serve to aid in the recognition of most cases with hypoglycemia secondary to hepatic derangement. The glucose tolerance curve in hepatic disease is of the high plateau type, similar to that seen in diabetes mellitus Roentgenologic examination may reveal a duodenal ulcer when symptoms are suspected as being related to this disease

The glucose tolerance test in the diagnosis of organic hyperinsulinism reveals variable results and its value is doubtful The value for fasting blood sugar gives more information than that of glucose tolerance tests A glucose tolerance test may show a subnormal fasting blood sugar. The blood sugar concentration rarely exceeds *120 mg per 100 ml during the test The blood sugar returns to subnormal* values within two hours, and its maintenance at low levels, usually throughout 3 to 6 hours after the test, is often observed The detection of an accelerated rate of removal of *glucose from the blood stream is diagnostically important In an adverse way the* glucose tolerance test may be of diagnostic importance, for in an hour or two after [illegible] occur

[illegible] *y the presence of a* blood sugar concentration of less than [illegible] mg per 100 ml of blood, or less than 40 mg per 100 ml. following restriction of carbohydrates or fasting plus exercise or during a spontaneous attack of hypoglycemia The *symptoms of hypoglycemia* are relieved by sugar, preferably given intravenously, and without the patient's knowledge of what is injected. In hyperinsulinism the glucose tolerance curve rises from hypoglycemic concentrations (60 mg per 100 ml of blood or less) to attain a concentration not in excess of 120 mg per 100 ml, falls again to subnormal levels within 2 hours and maintains the subnormal levels for from 3 to 6 hours. Hyperinsulinism is characterized by a progressive course, the attacks becoming more frequent and severe.

The preferred treatment is surgical removal Even in the presence of metastasis this may be required if for no other reason than for temporary *alleviation of the* hypoglycemia In some patients, however, the metastatic cells independently elaborate insulin, and the attacks of hypoglycemia will continue unabated even though the primary focus has been removed

TUMORS OF THE PANCREAS

There are benign tumors and primary and secondary malignant tumors of the pancreas, as well as a middle group of tumors of questionable genealogy and potentialities.

In an occasional case there will be minimal or no local symptoms of carcinoma of the pancreas. Recurring venous thrombi in various parts of the body begin to take place and their discovery initiates search for a primary malignant lesion which may be found in the pancreas

Examination. The liver is usually palpable Some enlargement of the liver is due to engorgement, and often hepatic metastasis is present. A distended gallbladder can be palpated clinically in about one half of these patients and the enlarged liver has no implications in regard to the presence or absence of jaundice The pancreas is relatively inaccessible to palpation A pancreatic mass is not commonly palpated. Splenic enlargement is rarely present

Ascites may develop as a result of (1) metastasis to the peritoneum or liver, and (2) thrombosis of the portal vein or (3) compression of the portal vein by lymph nodes or by malignant tissue

The disturbance of carbohydrate metabolism if present is manifested by glycosuria or hyperglycemia or by an impaired glucose tolerance, which is present in 4 of every 10 cases of primary pancreatic carcinoma. A combination of glycosuria, hyperglycemia and an impaired glucose tolerance may be demonstrated in 1 of every 3 cases.

The traditionally large, bulky, fermenting, fatty or greasy stools are seldom observed

Comfort and Osterberg employed determinations of both serum amylase and lipase. In their experience the serum lipase concentration was elevated in 40 per cent, while the serum amylase concentration was elevated in only 8 per cent of cases of carcinoma of the pancreas

Pancreatic secretion obtained with the use of a double-lumen gastroduodenal tube after the administration of secretin, mecholyl, or insulin will demonstrate some impairment in pancreatic secretory function There are diminished concentration of one or more of the enzymes, and reduction in total volume of secretion and lessened concentration of bicarbonate

In jaundiced patients the serum bilirubin concentration may have some value *in the differential diagnosis of pancreatic carcinoma and choledocholithiasis* In carcinoma the concentration is usually consistently greater, whereas in choledocholithiasis the concentration of bilirubin in the blood frequently fluctuates widely during a brief period of observation

Diagnosis A definite diagnosis can only be established by biopsy at the time of exploratory operation if the surgeon wishes to obtain the tissue, or by necropsy The roentgenologic examination of carcinoma of the pancreas yields indirect signs produced by the neoplasm on adjacent structures, particularly the duodenum

The diagnosis is often difficult and almost always is presumptive. It is particularly difficult when jaundice is not present or when either the body or the tail of the pancreas is predominantly involved The importance of demonstrating some impairment of carbohydrate metabolism and the value of roentgenograms and of determinations of concentration of pancreatic enzymes in the blood must be given due consideration When present, symptoms of painless jaundice, palpable distended gallbladder and fatty stools are significant

Carcinoma of the pancreas is a rapidly progressive disease. Death occurs on the average in 7 months after the first appearance of symptoms.

Sarcoma. Primary sarcomas of the pancreas are rare. These tumors commonly are solid Some are cystic The contents of the cysts are hemorrhagic and the walls are covered with bleeding nodular projections Apparently there is no predilection for any one part of the gland Local growth is rather rapid and the tumor may attain considerable size Metastatic extension, however, is not so widespread as in carcinoma The age incidence is similar to that of carcinoma and there is the same preponderance in males.

cause symptoms of pancreatic insufficiency consisting of large and bulky bowel motions which contain excess fat. In a few the symptoms of diabetes are present.

On examination there may be present an epigastric tumor, the size of which varies greatly; some tumors are so large as to occupy the greater part of the abdominal cavity. In 95 per cent of Judd, Mattson and Mahorner's patients the tumor was palpated above the umbilicus. Most cysts are spherical or dome-shaped with a smooth surface On palpation they are firm and resistant, but often fluctuation can be detected. As a rule, the mass does not move with respiration. On percussion the cyst will be flat with a zone of tympany intervening between it and the liver.

Roentgenologic examination, when due consideration is allowed for the history and the findings on physical examination, is frequently diagnostic However, a definite diagnosis can be made only on the basis of histologic study The diagnosis of pancreatic cysts is considered whenever there is present a tumor in the epigastric region of a middle-aged or an elderly patient, which has slowly enlarged and is not tender on palpation. Rarely are these tumors fluctuant to a detectable degree on palpation

The prognosis in most cases after surgical treatment of pancreatic cysts is good. If marsupialization is performed, a fistula may follow.

Malignant Tumors. *Carcinoma.* Of all the tumors of the pancreas, including benign and malignant growths, carcinoma is the commonest It is not a rare disease of middle-aged and aging individuals.

Most often the lesion is a scirrhous carcinoma, hard, nodular, and fixed on palpation, and of fibrous appearance when viewed grossly. These tumors are situated predominantly in the body and tail of the gland and tend to extend to massive involvement and to metastasize more widely than do the more rarely situated carcinomas of the head of the pancreas Carcinomas situated in the head of the pancreas often involve the lower end of the common duct, surrounding and compressing it, and invade the duodenum, the stomach and the colon.

The most frequent spread is to the liver through the portal vein From the liver the venous drainage may carry the cancer cells to the lungs and thence systemically to the adrenals, kidneys, spleen, bones and other structures including the brain. The posterior surface of the body of the pancreas lies directly over the celiac plexus and is immediately adjacent to the nerves entering and emerging from this plexus Severe abdominal pain may originate from extension along nerve sheaths.

SYMPTOMS Pancreatic carcinoma occurs most commonly in men in the sixth decade of life. It does occur in women and even in persons less than 20 years of age It has no racial preferences. Onset of symptoms of carcinoma of the pancreas may be ushered in by thrombophlebitis in a patient who has never had any venous trouble in the legs In most cases, however, the initial symptom is abdominal pain Commonly the disease commences with the so-called painless jaundice. However, patients who have so-called painless jaundice often suffer from varying degrees of pain.

Eusterman and Wilbur described the pain in their patients as follows of epigastric situation, extension around to the back, dull aching character, moderate severity, constant, steady progression, exaggeration at night and no relationship to normal events of the digestive cycle There is no constant type or location of pain which can be considered peculiar to pancreatic carcinoma The disease may begin with severe pain simulating that of acute cholecystitis or the pain of peptic ulcer The common complaints, such as loss of weight, anorexia, weakness, vomiting, diarrhea, and constipation are irregularly present

In some cases nausea and vomiting, suggestive of intestinal obstruction, are among the earliest manifestations of a primary pancreatic neoplasm In other cases local symptoms and signs are preceded by persistent diarrhea. Whenever a persistent diarrhea which cannot be accounted for afflicts a person of middle age, carcinoma of the pancreas should be suspected.

pause. A deficiency of the thyroid hormone tends to cause dysfunction of the reproductive system, inhibits estrus and counteracts the effects of estrone.

In the presence of thyroid deficiency there is an accumulation of water in the intracellular spaces. The administration of thyroid causes diuresis in the hypothyroid individual.

There is retention of calcium in hypothyroidism In hyperthyroidism, on the administration of thyroid there is an increased excretion of calcium and of phosphate without affecting the concentrations of the serum calcium and phosphorus However, in prolonged hyperthyroidism osteoporosis may be present

In the normal person administration of iodine stimulates the thyroid, whereas [illegible] paradoxical [illegible] the action [illegible] absence of nervous connections It has been assumed, however, that the apparent nervous control is mediated through the hypothalamic centers of the autonomic nervous system and thus in disease may affect the function of the gland

Diseases of the Thyroid Due to Congenital Malformations. The thyroid occasionally is involved in developmental defects The gland may be absent, as in sporadic cretinism. The thyroglossal tract, which normally is absorbed in early fetal life, may persist and give rise to thyroglossal cysts A high percentage of cures follows the radical excision (Sistrunk) of the entire thyroglossal tract (see Diseases of the Neck, Chapter 5)

Aberrant thyroid tissue may occur at the foramen cecum, where the thyroglossal duct normally ends, in interrupted masses along the original path of the duct, or in the thoracic cavity The last-named site must be kept in mind in cases of thyrotoxicosis in which there is no evidence of cervical enlargement Thyroid tissue may also be present in the ovary as the so-called ovarian struma Like the normally located gland, ectopic thyroidal tissue may give rise to hyperthyroidism

Cysts of the thyroid may be of congenital origin but they usually arise from hemorrhage into a follicle or from degenerative changes in an adenomatous nodule. *Hemorrhage* into a cyst, on the other hand, may result in thyroid apoplexy. In regions where nodular goiter is common, hemorrhages may occur early in life In older patients atherosclerotic changes may often be demonstrated in the arteries Rupture of these damaged thyroid vessels with resultant acute severe hemorrhage is uncommon but well recognized In their more severe form these hemorrhages are the principal cause of cyst formation The content of the larger cysts, and particularly of those developing within the mediastinum, is high in iron and low in iodine, indicating the hemorrhagic origin In hemorrhage into the thyroid gland there is a rapidly developing tumor, often there are fever and fast pulse if the hemorrhage be large In large hemorrhages pressure symptoms with resulting suffocation may develop and death ensue

Thyroiditis. Thyroiditis may occur as an acute, a subacute or a chronic infection occurring most commonly in middle aged women and rarely in men and children

Acute Thyroiditis. Inflammation of the thyroid gland is rare. When it does develop, it is usually during the course of acute infectious processes The gland becomes tender, enlarged, and may cause dyspnea and dysphagia. The inflammation usually subsides without suppuration or abscess formation

Subacute Thyroiditis. Subacute thyroiditis is a self-limited inflammation of the thyroid gland which may be initiated by a viral infection and prolonged by a granulomatous reaction to displaced or perverted colloid

In the past, subacute thyroiditis rarely was diagnosed, and therefore its true morbidity is not known In recent years it seems to have been diagnosed more frequently than formerly, but whether the greater number of diagnoses represents an

In general the symptoms are essentially those of carcinoma. Pain comprises the outstanding symptom, and jaundice is both a later appearing and less common manifestation. The tumor appears to be palpable oftener than is carcinoma. The other clinical, laboratory and roentgenologic features are no different from those observed in carcinoma and the course is as rapidly progressive

The diagnosis of sarcoma of the pancreas is made on the basis of biopsy or necropsy study. The prognosis is the same as that for carcinoma of the pancreas.

Malignant Cysts. *The relative incidence of malignant and benign pancreatic* cysts is about 1 malignant cyst for every 9 benign cysts True papillary cystadenocarcinoma is extremely rare in the pancreas Malignant cystic disease of the pancreas occurs equally in men and women in middle life The average age is 53 years.

If a pancreatic cyst displays a rapid increase in size or is unusually painful, *malignant change should be suspected*

On examination the most prominent finding is the presence of a large tumor. Within a short time re-examination reveals that the tumor is progressively increasing in size and is not tender. Loss of weight is an outstanding symptom.

The diagnosis is established by biopsy or necropsy studies The treatment is surgical Palliative marsupialization may be necessary when extirpation is impossible.

THE THYROID GLAND

The thyroid gland is a large, ductless organ in front of and on each side of the trachea *It is made up of two lateral lobes and an isthmus which unites the lobes below.* The gland is enclosed in a thin envelope of connective tissue, and is composed of a number of closed follicles, or alveoli, which usually are filled with colloid material, and are surrounded by a network of vessels which is supported by the interstitial connective tissue.

The average adult thyroid contains about 10 mg. of iodine. Iodine exists in the gland as inorganic iodide, 10 per cent, diiodotyrosine (precursor of thyroxin), 60 per cent: and thyroxin (the active principle of the gland) 30 per cent, which is elaborated by the thyroid directly into the blood

The secretion of thyroxin is regulated by the concentrations of thyroxin and iodides in the blood, by the thyrotropic hormone of the anterior pituitary gland and by the action of the sympathetic division of the autonomic nervous system

The selective absorption of iodides from the blood is well demonstrated by the administration of radioactive iodine (usually I^{131}) in a dose equivalent to the amount of iodide contained in a normal daily diet. The iodide is rapidly absorbed from the intestine and passes into the plasma, from which it is selectively taken up by the thyroid gland Often 20 per cent of the administered radioactive iodide will be in the thyroid at the end of 6 hours. A normal thyroid will collect 80 times more of the radioactive iodide than will other tissues of the body A hyperplastic gland may collect 2 to 4 times as much radioactive iodide as that collected by the normal gland There is a maximal point of absorption beyond which the thyroid will not absorb more iodide despite its concentration in the blood In myxedema the iodide uptake is negligible.

Thyroxin *objectively affects metabolism, circulation, muscles, reproductive organs,* and water metabolism and calcium exchange.

The administration of desiccated thyroid causes a *disturbance of the heat-regulating* center in the hypothalamus. The alimentary tolerance for glucose is diminished, as evidenced by the fact that glycosuria may follow the ingestion of a large dose of carbohydrate. Fat metabolism also is affected

The administration of thyroid extracts stimulates the circulation The increased circulatory rate is a reflex response to the increased metabolism. The cardiac output is increased with a generalized increase in the blood flow through the periphery.

Large doses of thyroid induce progressive muscular changes and, finally, muscular atrophy.

The size of the thyroid gland and its iodine metabolism increase at puberty, during menstruation and in pregnancy. The gland decreases in size after the meno-

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actual increase in the frequency of the disease, or whether it is due to better recognition, is not known.

It has been observed that subacute thyroiditis sometimes follows infections of the upper part of the respiratory tract, measles, malaria, and scarlet fever. The prolonged chronic inflammatory process observed in the thyroid gland may be the result of a foreign body reaction to colloid which escapes into tissue spaces when the cells lining the follicles are damaged by infection.

Subacute thyroiditis occurs most commonly in patients between 30 and 50 years of age. In Crile and Rumsey's series the mean age was 42 years. Only 5 of the 38 patients were men.

The inflammatory reaction usually involves the entire thyroid gland but may affect only a portion of a lobe The occurrence of subacute thyroiditis in an adenomatous or a previously abnormal gland is unusual.

There is moderate enlargement of the thyroid up to two or at most three times its normal size The capsule is thin and pale On cut section the involved region is seen to be abnormally white, avascular, and hard but pliable. Pathologically, subacute thyroiditis is differentiated from Riedel's struma by the fact that in the latter disease there is extensive involvement of all the surrounding structures In subacute thyroiditis the inflammatory process is limited to the thyroid gland

SYMPTOMS. The symptoms of subacute thyroiditis are variable, but Crile and Rumsey have separated the manifestations into two categories: (1) the acute fulminating type with fever, pain, exquisite thyroid tenderness and severe systemic symptoms, and (2) the chronic type, with little if any fever, slight pain, slight tenderness and insignificant systemic symptoms

Between these two extremes there are many forms which present all combinations and degrees of local and systemic reactions. Subacute thyroiditis is essentially a self-limited disease which eventually subsides without demonstrable damage to the thyroid

The symptoms commence with fatigue, weakness and lassitude. Temperatures often rising to 101 F (38.3 C), and occasionally to 104 F (40 C), accompany the acute phase, and a low-grade fever may be prolonged for weeks or even months Night sweats, chills, and loss of body weight may occur Patients may experience symptoms of pressure resembling globus hystericus, and may complain of unusual nervousness, tremor, weakness, excessive perspiration, heat intolerance and palpitation

During the acute phase of the disease a sore throat, pain on swallowing, and exquisite tenderness of the thyroid are experienced Pain usually extends behind the ear on the affected side and occasionally to the occiput, face or jaw Occasionally the pain may be so severe in the jaw or the throat that teeth may be pulled or tonsils removed in attempts to give relief

EXAMINATION. The thyroid gland is firm, tender, and usually diffusely enlarged to one and one-half or two times its normal size, but it is readily palpable because of its hardness In some the firmness and tenderness may appear as a localized process involving only the isthmus or part of a lobe On subsequent examinations [illegible]

ness at the onset

The pulse rate is uniformly elevated in the acute form of subacute thyroiditis but in the chronic type may be normal

The sedimentation rate of the blood is said to be extremely high. In subacute thyroiditis the thyroid takes up little or no radioactive iodine. Other laboratory tests are of little value The leukocyte count is not elevated The basal metabolic rate is not materially affected, but occasionally it will be increased In three fourths of the cases the basal metabolic rates are in the normal range of —10 to +10 per cent.

DIAGNOSIS. The diagnosis of subacute thyroiditis is predicated on the finding of a firm and tender thyroid gland during or subsequent to infections of the upper part of the respiratory tract, measles, malaria and scarlet fever. When the entire gland or one entire lobe is uniformly involved, the diagnosis usually is clear In the chronic phase, however, and especially when the thyroid is asymmetrically involved, it is difficult to establish the diagnosis unless there is a history of sore throat, persistent pain in the ear or jaw, or pain and tenderness over the thyroid gland at the onset of the disease. The presence of systemic symptoms further confirms the diagnosis.

Needle Biopsy. The diagnosis in questionable or obscure instances, according to Crile, may be greatly facilitated by biopsy Employment of the Vim-Silverman liver-biopsy needle has obviated the need for surgical exposure of the thyroid

Chronic Thyroiditis. Chronic thyroiditis is a rare condition occurring almost exclusively in middle-aged or elderly women.

Three types of chronic thyroiditis are recognized (1) In *Hashimoto's goiter* there is atrophy of the acini of the thyroid gland with replacement of the parenchymatous cells by a diffuse infiltration of lymphocytes This invasion of the thyroid by lymphocytes is only an exaggeration of what occasionally is seen in normal glands and commonly is found in exophthalmic and simple goiters The lymphocytes appear to fill regions in which degeneration or involution of the follicles occurs This form of thyroiditis responds well to irradiation (2) In *Riedel's goiter* there is replacement of the normal acinar tissue by dense fibrous connective tissue The gland becomes hard and may give symptoms due to pressure on the trachea and esophagus (3) In *struma fibrosa* there is fibrosis of the gland secondary to an acute or a chronic inflammatory process. The condition is characterized by the presence of pseudogiant cells giving the giant cell type of thyroiditis.

SYMPTOMS. Chronic thyroiditis generally follows a prolonged chronic course. It occurs in patients who give a history of chronic infection (for example, syphilis or respiratory disease). It is assumed that the thyroiditis is secondary to these infections or to vascular changes which induce nonspecific degenerative changes in the gland. The symptoms therefore are those of the original disease plus the effects of the enlarged, hardened gland pressing on the trachea.

Examination reveals the thyroid gland to be enlarged and hard, often it extends substernally.

The diagnosis of chronic thyroiditis is made on the basis of the foregoing description of the disease. Determination of the type of pathologic change requires microscopic study. In Hashimoto's disease the gland is symmetrically enlarged, but resilient. In Riedel's struma the normal shape of the gland is not retained, but its surface remains smooth, tender and not nodular This process tends to adhere to surrounding structures Riedel's struma may affect only part of a lobe Hashimoto's disease occurs almost entirely in women, Riedel's struma occurs also in men Either may occur at any age.

Goiter. Any enlargement of the thyroid gland is designated as a goiter. To differentiate the various types of goiter, the American Association for the Study of Goiter has adopted the following terminology and classification:

1 Nontoxic goiter
   a. diffuse (endemic and adolescent)
   b nodular (adenomatous and colloid)
2. Toxic goiter:
   a. diffuse (Graves' disease, primary hyperthyroidism)
   b. nodular (toxic adenoma, secondary hyperthyroidism)
3 Malignant goiter
4. Inflammatory disease (discussed earlier)

In diffuse nontoxic goiter there is a symmetric, soft enlargement which occurs most frequently at puberty, during pregnancy, or during other periods of stress.

The term toxic goiter implies that the thyroid makes available an excessive supply of utilizable thyroxin.

Nontoxic Goiters. *Simple or Endemic and Adolescent Goiter.* Simple goiter is a deficiency disease caused by a lack of a sufficient available supply or utilization of iodine There is enlargement of the thyroid without associated toxic manifestations.

This form of goiter is endemic and sporadic Endemic goiter occurs in well-defined geographic regions where iodine deficiency is prevalent. Inhabitants of mountainous regions are particularly likely to be goitrous. Thus in the Eastern United States the goiter belt extends along the Appalachian range, particularly along the eastern slopes of the Alleghenies. In the Ozark Mountains or Plateau (south central part) goiter is moderately endemic. On the West Coast goiter is encountered along the western slopes of the Rockies. In the north along the Great Lakes is a large endemic area for goiter.

In addition to the requirement of an optimal iodine concentration in the food and drink, a deficiency of vitamin A may induce goiter when the iodine intake is in the lower range of normality The goitrogenic effects of fats have also been demonstrated Poor sanitation, infections, avitaminosis, puberty and pregnancy increase the requirement for iodine and are conducive to the development of goiter.

During the early stages of the disease there is a diffuse enlargement of the gland, the follicles being distended with colloid (colloid goiter) As time passes, the simple goiter, either spontaneously or as the result of the administration of iodine, may be reduced to normal size or it may become atrophied In the atrophied gland the alveoli become distorted and compressed, and the epithelium remains high and irregularly arranged. In long-standing goiter the gland may become nodular. Most modules of the thyroid consist of follicles distended with colloid, others undergo cystic degeneration. Adenoma of the thyroid is commoner in nodular glands than in the normal, it may undergo malignant change and give rise to carcinoma

Girls and women are more prone to acquire the disease than are boys and men, and the goiter tends to become larger in females than in males The incidence in males reaches a maximum before the age of puberty, whereas in females maximal occurrence is present after puberty.

The goiter may become large without having attracted the attention of the patient Some patients may complain of symptoms that suggest pressure on the esophagus, trachea or recurrent laryngeal nerves.

On examination the thyroid gland is smooth, soft and enlarged throughout, the borders may be somewhat indistinct, there are no bruits or thrills. In boys in whom goiter develops before puberty the gland later may become smaller, but in girls such is not the rule In many the enlargement tends to fluctuate in size in proportion to various stresses, but slowly increases in size During pregnancy there is some enlargement of the thyroid gland With the approach of middle life the lesions often become nodular During the remainder of the patient's life the goiter tends to become larger and more nodular Thyrotoxic changes may occur. Malignant changes occur more frequently in association with nodules in the thyroid gland than in the diffusely enlarged gland Hemorrhage into a cyst may cause acute pain and swelling in the neck

The diagnosis is established by the presence of the enlarged thyroid gland In acute thyroiditis there is a history of recent onset of pain and swelling The mass is associated with tenderness, fever and leukocytosis The differentiation of diffuse endemic goiter present in a middle-aged person from carcinoma of the thyroid gland is impossible until histologic studies have been completed

Simple goiter, in its early stages, is readily curable by the administration of iodine.

Nodular (Adenomatous and Colloid) Goiter. The goiter of endemic and adolescent (simple goiter) origin is characterized in the early stages by a diffuse en-

largement of the thyroid gland. The follicles are distended with colloid—the colloid goiter. The gland apparently has undergone hyperplasia as a compensatory reaction to the lack of iodine

The hyperplastic thyroid gland of colloid goiter maintains a normal physiologic function despite its abnormal anatomic state. It may be looked on as a gland in the resting stage following active hyperplasia In some instances, however, the hyperplastic gland may undergo exhaustion atrophy, in which case the alveoli become distorted and compressed and the epithelium remains high and irregularly arranged With the advent of involution the accumulation of colloid in the involuted gland may also be termed colloid goiter. Hyperplasia and involution may be successively repeated

In long-standing goiter there is a tendency for the gland to become nodular This is explained by assuming that the stimulation of the gland is not always uniform, in which case a diffuse colloid goiter results If a localized region is stimulated, this tends to cause pressure atrophy of the surrounding cells and the formation of a fibrous capsule around it, thus giving rise to a nodule The disturbed activity of the cells also renders them more prone to undergo neoplastic change than normally functioning cells. Hence adenoma is much commoner in nodular thyroid glands than in normal thyroid glands The adenoma in turn may undergo malignant change and give rise to carcinoma. Most nodules of the thyroid consist of follicles distended with colloid (colloid nodules); others undergo cystic degeneration

Nodular goiter causes no symptoms unless it is very large or it is situated substernally Large substernal goiters are mediastinal tumors and they are thus manifested

On examination the nodules are palpated There may be one nodule or several nodules or, in some instances, one lobe or all of the lobes of the thyroid are involved

Diagnosis is established by palpation unless the adenoma is substernally situated and then it is diagnosed by roentgenologic examination

In the early stages of nodular goiter iodine may be therapeutically beneficial

ENDOCRINE DISORDERS OF THE THYROID

Hypothyroidism. A deficiency of the thyroid hormone is responsible for (1) cretinism when the deficiency occurs before birth or during infancy, (2) juvenile hypothyroidism when the deficiency is less profound and occurs during childhood, (3) hypothyroidism in the adult when the deficiency is partial and (4) myxedema when it is complete.

Cretinism. In regions in which goiter is endemic a condition characterized by dwarfism and imbecility is designated as cretinism. Two types of cretinism are de- [illegible] the endemic, [illegible] differences [illegible]

[illegible] the sporadic cretin there is failure of development of the thyroid In the cretin residing in an area of endemic goiter there may be a congenital absence of the thyroid gland, but usually there is degeneration of the thyroid in uterine life or in early infancy. The lack of iodine is the chief cause of cretinism, but a congenital absence of the thyroid or factors which cause destruction of the gland, such as infections or hereditary syphilis, may induce the disorder

Symptoms. The symptoms vary in accordance with the age at onset of the disease, the interval without therapy, and the severity of the disease. The brain of the cretin fails to develop properly and imbecility results. There are marked apathy, defective speech, a clumsy gait, incontinence and other evidence of maldevelopment of the neuromuscular system The cretin is a dull and placid idiot or imbecile Sitting,

walking and talking are considerably delayed. Often there are anorexia and constipation.

Examination The cretin is dwarfed owing to a delay in the appearance and lack of function of the ossification centers. The deficient growth of the sphenoid bone gives a characteristic depression at the root of the nose

The skin is thick, dry and cold; the hair is sparse or may *fall* out; the nails are thin and brittle, the teeth become carious early in life. The hands and feet are fat and the digits are short The lips are thick and dry The tongue is thick and protrudes through the open, gaping mouth, dribbling saliva. The cretin is very susceptible to infection and, like the mongolian idiot, may succumb easily to infection while young

Owing to hyaline degeneration, the muscles are flaccid The abdomen protrudes; umbilical hernias are frequent. There is a tendency toward adipose deposits about the hips and above the mons veneris Delayed dentition, pallor, and anemia and sexual infantilism are characteristic

Determinations of the basal metabolic rate are helpful, but not conveniently done because of the necessity of a special respiratory chamber A high serum cholesterol concentration and a low plasma protein-bound iodine are found Roentgenograms reveal delayed appearance of ossification centers.

Diagnosis The diagnosis of cretinism should be considered in any child showing delay in all phases of development Suggestive manifestations are delayed osseous development, mental retardation, bradycardia and hypothermia The various kinds of idiots and dwarfs are to be differentiated (see Dwarfishness, Chapter 16)

The mongolian idiot is more active than the cretin, has finer features, and has hypermobility of the joints The skin is warm and moist The wide spacing of the eyes in ocular hypertelorism may simulate cretinism because of dwarfism and mental deficiency. In mongolian idiots growth is not stunted and the basal metabolism is normal

The success of thyroid therapy in cretinism is dependent on the age at which it is begun, on the dosage and the duration of treatment, as well as on the severity of the disease It should be given a trial.

Juvenile Hypothyroidism. During childhood, in juvenile hypothyroidism, *thyroid insufficiency of a milder degree than that of the cretin is present*

There are many symptoms common to cretinism, juvenile myxedema, and adult myxedema. Prominent among these are stunting of growth, and mental retardation In juvenile hypothyroidism early development is normal, but later a great retardation ensues. *The genitalia are normal, but puberty is delayed*

Examination reveals the child to be small for its age The skin is dry and thick. The hair is dry, and the nails are brittle There is mental retardation

Examination in juvenile myxedema reveals a stunting of growth due to retardation in osseous development The retardation in osseous development with a resulting subnormal bone age, as determined by roentgenologic examination, is a characteristic feature of juvenile hypothyroidism There is usually present some abnormal ossification of the cartilages of the epiphyses and of the round bones (epiphyseal dysgenesis). The porous stippling of the cartilage observed in epiphyseal dysgenesis is not always present in hypothyroidism, and a similar appearance in the roentgenogram is observed in osteochondritis deformans and in chondrodystrophy The disturbance in ossification is particularly likely to affect the hip, and because of the similar appearance in the roentgenogram, may suggest osteochondritis deformans juvenilis (Legg-Perthes disease)

There are elevated cholesterol content of the blood, reduced basal metabolic rate, and subnormal rate of creatine excretion

The determinations of the basal metabolic rate and the rate of creatine excre-

tion are useful procedures in the diagnosis of hypothyroidism. The concentration of *cholesterol in the blood is frequently increased but may be within the normal limits.* However, as has been shown by Wilkins, the cholesterol level uniformly rises after the cessation of thyroid therapy.

Hypothyroidism in the Adult. In the adult, hypothyroidism when complete gives rise to a characteristic syndrome designated as myxedema The milder forms of hypothyroidism in the adult are difficult to recognize, for the early degrees of hypothyroidism give but few vague symptoms, which are suggestive of a psychoneurosis. The presence of a basal metabolic rate of −20 to −30 per cent is significant.

***Myxedema** (Gull's Disease)* Myxedema is a moderately rare disease It occurs 4 out of every 5 times in women

Of the causes of myxedema, the excessive administration of thyroid extracts and goitrogenic compounds, the use of radioiodine and roentgen rays, thyroidectomy, and thyroiditis are common. Spontaneous occurrences are observed

Marked atrophy of the thyroid gland occurs in Simmonds' disease because of hypothyrotropinism The majority of patients with thyroid atrophy, however, do not have panhypopituitarism. That the pituitary is not deficient in some instances is indicated by the presence of an excessive amount of thyrotropin in the blood and urine of some patients who have myxedema

The hypothyroidism found in patients who have undergone thyroidectomy or radioiodotherapeusis results from removal or injury of an excessive amount of thyroid tissue

The various goitrogenic agents produce myxedema either by preventing the gland from concentrating iodide or by interfering with the utilization of iodide in the synthesis of thyroxin, as exemplified by thiouracil. On withdrawal of ingestion of the antithyroid agent, the myxedema usually disappears

With extensive inflammatory changes in the thyroid, such as occur in severe forms of thyroiditis, so much of the acinar tissue may be destroyed that myxedema ensues.

In myxedema there is often an infiltration of the thyroid gland by connective tissue and lymphocytic cells which replace the glandular epithelium In primary myxedema there is no evidence of pituitary insufficiency Chronic thyroiditis and hyperthyroidism may *terminate in myxedema Otherwise the factors responsible for the condition are* obscure and usually unknown.

Myxedema commences insidiously The patient observes a thick dry skin and a puffed face, particularly the upper lids which seem heavy and enlarged There are complaints of inability of mental concentration, fatigue, slow and awkward movements, *drowsiness, muscular stiffness, falling hair and inability to get around quickly.* The patient is aware of but is not concerned about the lack of emotional response Myxedema is the only known disease in which otherwise normal young men and women will admit of decrease of libido and impotence without concern

Patients who have mild degrees of hypothyroidism may complain of a constant ache or pain in the chest which is aggravated by effort The anginal pain in myxedema is often secondary to the arteriosclerosis of the coronary vessels which is common among myxedematous patients beyond middle life. It is this form of angina that is relieved by thyroid therapy, angina due to intrinsic heart disease is aggravated by such therapy.

The tongue is thickened enough to interfere with the speech, which is slow, owing to difficulty in enunciation, and is bass and husky. The voice and speech of the myxedematous patient characteristically simulate the voice and speech of one who has acute alcoholic intoxication.

The face lacks expression when quiet, but this may not be apparent when the patient talks. The nose thickens and the cheeks are flabby. The fingers are short and stubby The teeth loosen and fall out Owing to puffy upper eyelids the palpebral fissures appear small Deafness may be found as a result of swelling of the larynx and tympanic membrane

walking and talking are considerably delayed. Often there are anorexia and constipation.

EXAMINATION The cretin is dwarfed owing to a delay in the appearance and lack of function of the ossification centers. The deficient growth of the sphenoid bone gives a characteristic depression at the root of the nose

The skin is thick, dry and cold; the hair is sparse or may fall out, the nails are thin and brittle, the teeth become carious early in life. The hands and feet are fat and the digits are short. The lips are thick and dry The tongue is thick and protrudes through the open, gaping mouth, dribbling saliva. The cretin is very susceptible to infection and, like the mongolian idiot, may succumb easily to infection while young

Owing to hyaline degeneration, the muscles are flaccid The abdomen protrudes, umbilical hernias *are frequent There is a tendency toward adipose deposits about* the hips and above the mons veneris. Delayed dentition, pallor, and anemia and sexual infantilism are characteristic

Determinations of the basal metabolic rate are helpful, but not conveniently done because of the necessity of a special respiratory chamber A high serum cholesterol concentration and a low plasma protein-bound iodine are found. Roentgenograms reve[illegible]

DIAGNOSIS [illegible]
delay in all pha[illegible]
development, m[illegible]
of idiots and dwarfs are to be differentiated (see Dwarfishness, Chapter 16)

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There are elevated cholesterol content of the blood, reduced basal metabolic rate, and subnormal rate of creatine excretion.

The determinations of the basal metabolic rate and the rate of creatine excre-

adenoma, or adenomas, which give rise to the observed symptoms. In diffuse goiter the hyperactivity of the thyroid is believed to be secondary to some unknown extrathyroidal abnormal stimulus.

Toxic Adenoma. Toxic adenoma of the thyroid gland usually occurs in middle-aged women and elderly patients The nodular growth and the toxic adenoma are the manifestations of endemic goiter, whereas hyperthyroidism occurs throughout the general population In regions of endemic goiter the repeated hyperplasia and involution to which the gland is exposed are the result of iodine deficiency which predisposes to the development of adenoma

In adenoma of the thyroid there is a proliferation of tissue in well-defined, circumscribed and encapsulated masses seen in adenomas of other tissues. Both nodules and adenomas occur in the thyroid gland. The nodule is the most commonly encountered; it is simply a region of colloid hyperplasia. The adenoma is a true neoplastic growth. Adenomas are divided clinically into benign and toxic types, depending on the symptoms present It is impossible, except by histologic methods, to distinguish a simple nodule from an adenoma

Pathologists may classify adenomas of the thyroid as papillary, fetal and simple colloid goiters. There is little clinical value to be derived from such a classification

A toxic adenoma originates the symptoms of thyrotoxicosis without exophthalmos and abnormal psychic disturbances The symptoms of hyperthyroidism are considered in the discussion of exophthalmic goiter in this text.

Toxic adenoma of the thyroid is often the cause of heart disease and of congestive heart failure Heart failure is due solely to cardiac overwork induced by the elevated metabolism and increased demand on the cardiovascular system

In thyrotoxic heart disease the symptoms of hyperthyroidism may be masked entirely by cardiac failure The determination of the basal metabolic rate in these cases is of little significance, for, in the presence of congestive heart failure, this may [illegible]

[illegible]

goiter or Graves' disease occurs uniformly throughout the population Its incidence is the same in regions of endemic goiter and in regions where endemic goiter does not prevail There is an opinion abroad that endemic goiter and exophthalmic goiter are etiologically different Exophthalmic goiter is rare in tropical and subtropical areas It is commoner in urban than in rural populations No race is immune to it. Epidemics have been described

Exophthalmic goiter affects women 10 to 15 times more frequently than men It usually becomes evident after puberty. However, children and even infants may have the disease

There is a familial tendency and the disease is commonest in those in whom there is a family history of neurosis and psychosis There is a strong clinical impression too that often there may be a constitutional predisposition which when combined with an environmental maladjustment results in hyperthyroidism

In an overactive thyroid gland the blood supply is increased The colloid becomes thinner and disappears, being replaced by a thin fluid which stains poorly with eosin. The epithelial cells become columnar. The alveoli enlarge, papillary infoldings of the [illegible]

[illegible] hyperthyroidism are goiter, exophthalmos, tremor and tachycardia. However, in some instances the goiter may be hard to demonstrate These manifestations in association with other symptoms—irritability, purposeless movements, hyperhidrosis, loss of body weight, dyspnea,

the glabrous skin. The hair is dry, brittle, without gloss, and grows slowly. Fingernails tend to be brittle

The skin is cool, dry, rough, scaly, atrophic, inelastic and puffy. In the early phases of the disease there is no pitting of the skin although it is definitely swollen Cutaneous wounds heal slowly In an occasional patient marked accumulations of desquamated skin may form thick crusts In a few patients the skin is smooth and glistening

The thyroid gland usually is impalpable, but occasionally it is enlarged. In such instances there usually is thyroiditis, or an endemic goiter or malignancy present.

The pulse rate and occasionally the pulse pressure are decreased Hypertension often is present in the myxedematous patient Occasionally there is hypotension Fluids tend to accumulate in the serosal cavities in patients who have had myxedema for a long time Congestive heart failure is infrequent in the absence of intrinsic heart disease The heart sounds are distant Electrocardiograms show a decrease in the amplitude of the complexes; flattening of the T waves is particularly common.

Slight atrophy of the gonads is observed occasionally Usually there is a decrease in libido and fertility Impotence is common in men

Slow mentation is one of the most characteristic manifestations. Comprehension is markedly impaired and there is a decrease in the perceptibility of general and special sensory stimuli Drowsiness and stupor are often present, but instead there may occasionally be nervousness and apprehension

There may be a decrease in the plasma volume and an increase in the concentration of protein

In myxedema the total cholesterol, cholesterol esters and phospholipid of the plasma may be increased The protein-bound iodine of the plasma is usually less than 3 5 micrograms per 100 ml In myxedema no concentration of radioiodine is found in the thyroid region Moreover, the patients usually excrete more of the isotope in 24 hours than do euthyroid or hyperthyroid persons

The urine may be scant in quantity and albuminous

DIAGNOSIS The basal metabolic rate of patients with fully developed myxedema is usually between −30 and −40 per cent In a few patients who have heart disease, infection or other condition as a complication, the basal rate may not be less than −15 per cent, even though the clinical manifestations of myxedema seem clear

A therapeutic test with desiccated thyroid is sometimes of advantage in patients who look and act myxedematous, who cannot take a satisfactory basal metabolism test, and who have a normal serum cholesterol When the patient has myxedema, a clear-cut clinical response is obtained within 3 weeks after administration of standard doses of thyroid It is not usually necessary to test by means of radioiodine

Toxic Goiter: Hyperthyroidism or Thyrotoxicosis. Hyperthyroidism may be produced by the administration of thyroxin Hyperthyroidism occurs clinically as the result of (1) an excessive secretion of thyroxin by adenomatous nodules, single or multiple, in the thyroid gland or in aberrant thyroid tissue (struma ovarii) and (2) diffuse overactivity of the thyroid gland In the first instance the hyperthyroidism is designated as due to toxic adenoma, and in the second instance the hyperthyroidism is termed exophthalmic goiter

Hyperthyroidism results from a variety of unknown mechanisms which have in common an exaggeration of the normal secretory activity of the thyroid The gland responds to these unknown mechanisms with an exaggerated secretion which in turn gives rise to most of the symptoms, while some of the symptoms are due only partly (exophthalmos) or perhaps not at all to the overactivity of the gland In every instance the term hyperthyroidism indicates an overactivity of the gland with production of an excess of the thyroid hormone The term toxic does not imply the production of an abnormal secretion by the entire gland

In toxic adenomatous goiter the thyroid is the site of a hyperfunctioning

The changes in the skin constitute one of the most characteristic aspects of the disease. In thyrotoxicosis the hands are usually warm and moist, but they may be cold and moist, as is observed in neurocirculatory asthenia The glabrous skin is flushed, hot, moist, fine and smooth The cutaneous alterations result chiefly from the increased peripheral circulation and perspiration and the increased dissipation of heat.

There is a weakness of the voluntary muscles in hyperthyroidism The leg muscles are often too weak for the patient to ascend one step upward to the examining table. In an occasional patient there is a degree of muscular atrophy, weakness and reflex changes which simulate progressive muscular atrophy. Myasthenia secondary to thyrotoxicosis may or may not respond to neostigmine, whereas primary myasthenia usually responds With the production of a complete remission of thyrotoxicosis, some of these myopathies become milder while others are unimproved or worsen. Comparable myopathies may occur at the time of the menopause with or without hyperthyroidism

The fingers show a rapid, finely vibratory tremor when they are voluntarily spread apart The tremor of hyperthyroidism is not distinctive A comparable form of vibratory tremor may be present in tense individuals who do not have hyperthyroidism The tremor of hyperthyroidism is of low amplitude and always of high frequency. Moreover, psychic instability is not helpful in distinguishing the tremor of hyperthyroidism, for all of those who have fine tremors are unstable individuals

The nails and scalp hair tend to be friable A decrease or absence of axillary hair is found in many of these patients, this phenomenon usually antedates the thyrotoxicosis

The reflexes in almost all thyrotoxic individuals are markedly hyperactive The required time for the performance of many activities is increased despite the apparent nimbleness of locomotor action

An increase in the pulse volume, resulting from an increase in the systolic blood pressure, is common The systolic blood pressure is increased to 160 or 170 measured in millimeters of mercury The diastolic blood pressure remains unchanged.

Pulse rates from 90 to 110 are common Auricular fibrillation is present in some patients; occasionally auricular flutter is found The heart contractions are forceful. There is increased cardiac output, accomplished by an increase in rate and stroke volume Systolic murmurs are frequent

Congestive heart failure occurs commonly with thyrotoxicosis, particularly in the older age group. Often the congestive failure is unrelated to the hyperthyroidism except for the extra load placed on the heart by the thyrotoxicosis

When ocular changes are associated with hyperthyroidism, these changes consist of a widening of the palpebral fissures, exophthalmos and a stare The degree of widening of the palpebral fissures and the amount of exophthalmos vary with emotional stress There is a lid lag on downward rotation of the eyeballs; convergence is poor.

On examination, lid lag or von Graefe's sign is manifested by a failure of the upper lid to follow the eyeball steadily downward when the gaze is directed slowly downward by following a gradually lowered finger. The sclera shows above the iris

Leukopenia may be present The total leukocyte count is occasionally found to be as low as 3,200 *per* cubic millimeter. Not infrequently there are granulocytopenia, lymphocytosis and monocytosis

The plasma volume is increased, attributable chiefly to an increase in water. The concentration of serum protein is decreased slightly Hyperglycemia and decreased

presented. Some patients do not complain of illness. It is the appearance of exophthalmos or loss of weight, noticed by the family, or a tremor interfering with work which may force the patient to seek relief.

The increased requirement for food stimulates the appetite. The hyperphagia, however, does not usually compensate for the hypermetabolism, and loss of weight ensues. The amount of weight lost varies from 1 pound to more than 100 pounds A loss of from 10 to 30 pounds occurs with great regularity.

Acute emotional upsets due, for example, to an automobile accident, or a sudden death in the family, seem to precipitate the symptoms. In other instances there may be a long period of stress and anxiety such as a prolonged illness in the family. However, emotional strain plays only a contributory role, for in only a very small proportion of persons experiencing psychic trauma does thyrotoxicosis ensue

Often there is a simultaneous appearance of restlessness, palpitation, intolerance of heat, and increased appetite In a few there may be a sudden onset of severe diarrhea, which the patient cannot relate to a specific item of diet. In still others all of the disturbances may be manifested by the cardiovascular system In rare instances psychosis or myopathy with great muscular weakness is the first symptom to develop The symptoms may subside to recur at intervals for years. In some the symptoms may disappear spontaneously. Some patients do not seem to be disturbed by the symptoms until some complication of the disease forces them to be aware. A few patients maintain that they feel much better when they are mildly hyperthyroid than when they are euthyroid This is more frequently observed in those who have heart failure

These patients are "nervous" and prone to have psychoneurosis and "nervous breakdown." Agitation, delirium and other forms of toxic psychoses develop easily. Manic-depressive states, schizophrenia and paranoid reactions are observed in a great many of these patients It is probable, however, that most of these psychic states are already present and are intensified by the thyrotoxicosis

In women the menstrual flow tends to be scanty and infrequent Estrogen antagonizes thyroid function by inhibiting the production of thyrotropin. Testosterone tends to stimulate the thyroid and to increase the metabolic rate

Almost all of the patients complain of increased sensitivity and decreased tolerance to heat They are comfortable in lower temperatures when the room or weather is hot (above 65 F) They tend to wear fewer clothes, use less bed covering, put their feet from under the covers, and want less heat in their rooms than do persons in normal health

There are many unrestrained emotional surges There may be silly outbursts of laughter, loquacity, euphoria and great exuberance Weeping is common, usually appearing spontaneously and sometimes to the disgust of the patient

The patient may complain that the eyeballs begin to protrude (exophthalmos). The protruding eyeballs give the patient an appearance of surprise or terror and the discomforts of chronic conjunctivitis

CRISES. Sometimes in the course of exophthalmic goiter or in toxic adenoma a crisis may occur. The crisis consists of severe psychomotor reactions, protracted vomiting, oliguria, tachycardia, hyperpyrexia and an elevation of the blood pressure, both systolic and diastolic The crises or the fulminating form of hyperthyroidism may arise after the discontinuance of iodine therapy, or after thyroidectomy On rare occasions a crisis will occur in a patient who has minimal or no recognized symptoms of hyperthyroidism

EXAMINATION. The peripheral [illegible]

are dilated

symptoms of thyrotoxicity. The oculopathy varies considerably in different patients In a few the ocular symptoms may be much more troublesome than the thyrotoxicosis, even though the latter is severe Long-continued exophthalmos may lead to ulceration, extrusion of the lens, or panophthalmia The severe orbital complications have been designated as malignant exophthalmos, exophthalmic ophthalmoplegia, and hyperophthalmopathic hyperthyroidism

Malignant exophthalmos develops either spontaneously or after thyroidectomy The etiology of this type of exophthalmos is different from that of the exophthalmos seen in thyrotoxicosis. It is a distinct syndrome The term malignant exophthalmos is supposed to cover a group of cases in which exophthalmos and loss of ocular movement occur together, sometimes associated with, at others independently of, thyrotoxicosis. Patients who have the spontaneous type are not improved by surgical removal of the thyroid.

The exophthalmos-promoting effect of anterior lobe of the pituitary body is brought about by action on other end-organs than the thyroid gland The knowledge of such experimental data is the origin of the term thyrotropic or pituitary type of exophthalmos.

The characteristic syndrome is varying degrees of exophthalmos and paralysis limited to ocular muscles and engorged conjunctivae (see p 125)

MALIGNANT TUMORS

Malignant tumors of the thyroid gland are less common than are benign tumors (adenomas). Malignant tumors of the thyroid usually do not give rise to any important symptoms that can be attributed to hyperthyroidism or hypothyroidism

Adenocarcinoma constitutes 9 of every 10 of all malignant lesions of the gland. Sarcoma of the thyroid may originate in the lymphatic tissue (lymphosarcoma) or in the stroma or capsule (spindle cell sarcoma or fibrosarcoma)

Some adenocarcinomas of the thyroid manifest a low grade of malignancy, so much so that both the adenoma and its metastatic growths resemble benign adenoma These tumors have been designated malignant adenoma and benign metastasizing adenoma. They are best designated adenocarcinoma, grade I (Broders) A similar tendency to low-grade malignancy is sometimes present in the lateral aberrant thyroid tissues

In 8 of every 10 cases adenocarcinoma originates in adenomatous nodules of the thyroid gland as the result of malignant changes

The adenocarcinomas may be divided into the papillary and diffuse types Scirrhous carcinoma and mixed carcinoma and sarcoma rarely are observed

An adenocarcinoma in the thyroid may remain localized for a long time before it metastasizes. The metastasis is by direct extension or by lymphatic invasion to the cervical lymph nodes or into the mediastinum or by extension into the veins with metastasis to the bones, lungs or brain Carcinoma of the thyroid may metastasize by way of the blood stream. The process is progressive and debilitating

The incidence of carcinoma in nodular goiter varies somewhat in different sections of the country and in different reports It is about 4 per cent

There is considerable variation in the age of the patients who have carcinoma of the thyroid Pemberton and Lovelace recorded an average age of 48.1 years in women and 52.8 years in men There seems to be some evidence that as the diagnosis and thus the incidence of cancer increases, the tumor afflicts younger persons. Carcinoma of the thyroid, unlike carcinoma in most other organs, may appear in young people, including children In 62 children 14 years of age or less who had nodular goiter, Kennedy reported carcinoma present in 12. All these carcinomas were in nontoxic nodular glands

Goiter of all types is commoner in women than in men. The incidence of carcinoma of the thyroid is higher in men than in women. The incidence of nodular goiter is higher in women.

The incidence of carcinoma of the thyroid is much higher in nontoxic nodular

glucose tolerance are found more commonly than in the average euthyroid patient There is a tendency to polyuria and an increased excretion of nitrogen, phosphorus, calcium, potassium, sodium, chloride and creatine. Glycosuria is observed occasionally. [illegible]

There [illegible]
disease, c [illegible]
function of the pituitary perhaps contribute to the abnormal dextrose tolerance reactions. Diabetes among patients who have thyrotoxicosis is twice as common as among the general population. In some patients who have thyrotoxicosis, hyperglycemia and glycosuria disappear after a complete remission The diabetic patient who has thyrotoxicosis has difficulty in controlling the diabetes and often has insulin reactions.

DIAGNOSIS. The presence of goiter, exophthalmos, rapid heart action and tremor is sufficient evidence for a clinical diagnosis of hyperthyroidism Add to any one or any combination of these symptoms a definitely increased basal metabolic rate, and the diagnosis of hyperthyroidism is reasonably certain. In mild degrees of hyperthyroidism a period of observation accompanied by a series of basal metabolic determinations may be necessary An increased basal metabolic rate alone is not sufficient for the diagnosis of hyperthyroidism.

Hyperthyroidism Without Apparent Hypermetabolism. Patients who have diffuse and nodular goiter and who have a normal basal metabolic rate may have an increased serum iodine concentration. However, detailed iodine tolerance tests and the relatively high incidence of elevated values of serum iodine in euthyroid persons make it difficult to accept serum iodine concentration as a final diagnostic criterion for hyperthyroidism in individual patients Moreover, the clinical differentiation between hyperthyroidism and anxiety, chronic alcoholism or other psychoneurotic states has made for skepticism toward a diagnosis of apparent hyperthyroidism unless there is more evidence than increased concentration of serum iodides at hand.

In order to be more certain of the presence of hyperthyroidism without hypermetabolism, Werner and Hamilton required a definite response to therapy in addition to laboratory evidence from the radioiodine tracer, serum precipitable iodine and basal metabolic rate determinations before making a final diagnosis of hyperthyroidism without apparent hypermetabolism All patients were seen by Werner either in the hospital or in the thyroid clinic Adequate follow-up was possible after initiation of therapy in all but 1 case. The data in this case were included in the authors' tables since there was little doubt as to the correctness of the diagnosis It seems, therefore, that in rare instances hyperthyroidism without apparent hypermetabolism may exist. However, it seems better to ignore this diagnostic possibility and not to treat any patient for hyperthyroidism who does not have hypermetabolism

Exophthalmos and Thyrotoxicosis. Chronic progressive exophthalmos in thyrotoxicosis is a highly complex phenomenon, its cause has not been completely elucidated. This exophthalmos may show considerable variation from day to day in its early stages The degenerative and inflammatory changes and edema present in the orbital contents are the result rather than the cause of the exophthalmos

Exophthalmos accompanies hyperthyroidism but does not necessarily parallel it. Often it is absent but it may appear after subtotal thyroidectomy. Exophthalmos may make its first appearance, and may progress, even when the basal metabolic rate is low. When rapidly progressive, an exophthalmos may become so severe as to threaten vision by exposure of the cornea, by papilledema, and by changes in the optic nerve. Unilateral exophthalmos may occur in hyperthyroidism, and if so the right eye is more often affected than the left eye The presence of an orbital tumor should be excluded in all those who have unilateral exophthalmos.

The majority of patients exhibit orbital changes, which usually appear with the

with the normal state. In hyperthyroidism relatively large amounts of this element are taken up by the gland.

Radioactive Iodine. The normal range of radioiodine uptake by the thyroid gland is from 10 per cent to 25 per cent. Radioiodine uptake levels below 10 per cent are considered low (myxedema), between 30 and 50 per cent borderline, and in hyperthyroidism 50 to 80 per cent, of the total dose will be stored in the gland in 24 hours. The usual tracer dose is 100 microcuries of I^{131}

Antithyroid medication gives a false normal uptake value A strong iodine solution or propylthiouracil, recent roentgenologic examinations such as cholecystography, intravenous pyelography or injections of iodized oil will give false normal uptake in the radioiodine values Radiopaque substances *containing iodine administered for roentgenologic* study may cause high blood iodine levels as long as 2 or more years afterward

Radioactive iodine (I^{131}) is useful in diagnostic studies of the biosynthesis of the thyroid hormone, the role of the thyrotropic hormone of the pituitary gland, and the action of goitrogens, as well as the functioning capacity of thyroid tumors. With proper shielding of the Geiger-Muller tube the individual lobes of the thyroid and parts thereof, as well as aberrant and intrathoracic extensions of the thyroid and solitary nodules in one of the thyroid lobes, can be formed Similar use has been made of radioactive iodine uptake in the diagnosis of a lingual thyroid The recently introduced scintillating counter seems to be superior to the Geiger-Muller tube

The diagnostic value of radioactive iodine depends on the measurement of the fraction of the tracer dose collected by the thyroid gland, the determination of blood concentrations of radioactive iodine in a given period of time after the administration of a test dose, and the determination of the rate and degree of urinary excretion of radioactive iodine. The difference in these results in various disorders of thyroid function may give precise information of diagnostic value Following the ingestion of a test dose, radioactive iodine disappears from the blood most nearly completely in cases of hyperthyroidism, least nearly completely in hypothyroidism Euthyroidism falls somewhere between these extremes. Eight hours after ingestion the mean concentration of radioactive iodine in the serum of hyperthyroid patients may be 0 5 per cent of the test dose per liter, 1 0 per cent in euthyroid individuals, and 2 per cent in patients with myxedema The exponential rate of disappearance of radioactive iodine from the blood in hyperthyroidism is about 40 per cent per hour, in euthyroidism 17 per cent per hour, while in myxedema it may be about 9 per cent per hour

Twenty per cent of an administered dose of radioactive iodine is excreted in the urine in hyperthyroidism, 60 per cent in euthyroidism, and 90 per cent of the dose is excreted in the urine in hypothyroidism by the end of a 72 hour period provided there is normal renal function.

The concentration of radioactive iodine in the blood that is bound to protein reaches about 75 per cent or more of the ingested dose in 24 hours in hyperthyroid patients, is less than 45 per cent of the ingested dose in euthyroid persons, and is negligible in patients who have myxedema

In summary: An overactive thyroid gland promptly collects a large part of administered radioactive iodine. The gland utilizes this iodine in the formation of thyroid hormones. As the result of the protein binding, less iodine is lost in the urine. The processes in the case of hypothyroidism are the converse.

The methods for the determination of protein-bound iodine are technically difficult and often uncertain The use of radioactive iodine requires acquired skill in the use of technical apparatus which is not generally available

Determination of the basal metabolic rate remains the most practical method for determination of the status of thyroid activity available for clinical use.

THE BASAL METABOLIC RATE

The Basal Metabolic Rate. Determining the basal metabolic rate is an integral part of the evaluation of the thyroid disease About 75 per cent of persons without thyroid disease have a basal metabolism within the limits +10 to −10 per cent Ninety-five per cent will have a rate within the limits of +15 to −15 per cent (Boothby and Sandiford using DuBois standards). Aside from thyroid disorders there are many condi-

goiter than in toxic nodular goiter. The solitary nodule is much more dangerou from the standpoint of malignant change than in the multinodular gland The rela tionship of fetal adenomas to the genesis of malignant disease of the thyroid canno be stated

Often the patient is unaware of any symptoms or that there is a tumor of th thyroid In other instances there is a history of a sudden or gradual growth durin the several months immediately preceding the time when the patient sought medica aid Often the symptoms bringing the patient to the physician are voice change difficulty in swallowing or breathing, or some other manifestation of extension o the malignant process beyond the thyroid gland A common early symptom is a choking sensation which frequently awakes the patient from sleep.

As the tumor grows, there is evidence of pressure, with interference in respiration, and pain and swelling of the neck These symptoms may also be produced by benign growths. The symptoms of nontoxic and mildly toxic malignant goiter are so meager that it may be impossible to identify one from the other Such symptoms as slight nervousness, tachycardia, weakness, dyspnea and increase in sweating which have developed insidiously may be so mild that they are scarcely appreciated by the patient until after operation, when pronounced improvement ensues

In the early course of carcinoma of the thyroid palpation reveals a nodular tumor or tumors of the gland The sense of touch is not acute enough to permit diagnosis of malignancy by the degree of hardness of the tumor Later, when there is fixation of the thyroid to surrounding structures, and when metastasis has occurred, the physical findings are suggestive

The diagnosis of malignancy of the thyroid gland is established by histologic examination Any adenoma of the thyroid which suddenly begins rapid growth and produces pressure symptoms suggests malignancy The hard gland of Riedel's thyroiditis or the gland of Hashimoto's struma is easily differentiated from carcinoma by the fact that the normal anatomic shape of the gland is preserved in these conditions in contrast with the distortion observed in carcinoma

IODINE, PROTEIN-BOUND IODINE, AND RADIOACTIVE IODINE IN THE DIAGNOSIS OF DISORDERS OF THE THYROID GLAND

Iodine in the Blood. Human blood maintains a rather constant iodine content which ranges between 3 and 20 micrograms per *100 ml* *The concentration of iodine in* the blood is a rough measure of the release of the thyroid hormone The concentration varies with the geographic area in which the individual resides and with the method of determination Blood iodine is increased by gestation normally and in toxic nodular goiter and exophthalmic goiter In hypothyroidism the whole-blood iodine is often within normal limits whereas the acetone-insoluble fraction, the protein-bound iodine, which probably represents the iodine of the thyroid hormone, is diminished to about one half of its normal concentration

Protein-bound Iodine. Protein-bound iodine values in the blood of less than 5 micrograms per 100 *ml* are considered low, and those of more than 7 micrograms per 100 ml are considered high

Between overt myxedema and hyperthyroidism is normal thyroid activity or euthyroidism In many instances, in order to prove that euthyroidism prevails, extensive metabolic studies are necessary In cases of doubt, the determination of the protein-bound iodine and studies of radioactive iodine may be of diagnostic value

In nontoxic nodular goiter there is a linear relationship between the basal metabolic rate and the protein-bound iodine and also there is a significant relationship between the level of the protein-bound iodine and the duration of the goiter

The radioactive isotope of iodine is useful in studying the metabolism of iodine, for the gamma rays emitted from it can be detected by the Geiger counter. In this way the course of administered iodine may be followed in the intact organism. In hypothyroidism without goiter only small amounts of iodine are concentrated in the gland as compared

The functions of the parathyroid glands may be affected by developmental abnormalities or manifested by excess or insufficient secretion by the glands.

Parathyroid Insufficiency [illegible]

parathyroid glands as a result of operations on the thyroid gland

The symptoms of mild parathyroid insufficiency may commence with tingling sensations in the hands and feet, stiffness, dysphagia, fibrillary twitchings, constricted feeling in the throat, dyspnea, fatigue, muscular weakness, and gastrointestinal irritability. As the disease progresses, psychotic symptoms and convulsive seizures may ensue. In some a toxic delirium with anxiety, depression, hallucinations and dementia is present.

A characteristic symptom or series of symptoms is tetany (see Tetany in Chapter 22). In parathyroid tetany there is an increased susceptibility of the nervous system to external stimuli (see Strychnine Poisoning in Chapter 19, and Infections by *Clostridium tetani* in Chapter 6) Ordinarily insignificant stimuli such as tapping on a muscle or groups of muscles with a finger may cause a painful tonic spasm of the musculature. Carpopedal spasm, laryngospasm and convulsions are frequently subjects of complaint.

In chronic tetany, paresthesia is the most constant symptom It may be associated with nervousness, weakness and fatigue upon which are superimposed occasional attacks of carpal spasm and the other manifestations of acute tetany When it is long-continued, chronic tetany results in trophic changes such as softening of the teeth, poor healing of fractures, fragility of the nails, cataracts, loss of hair, and cutaneous changes.

On examination there may be no obvious evidence of tetany, for it may be latent. Latent tetany may be elicited by either mechanical or electrical stimuli

There are certain physical signs which may be elicited in latent tetany (1) Chvostek's sign is elicited by tapping the skin, thereby stimulating the facial nerve just anterior to the external auditory meatus A twitching of the facial muscles is Chvostek's phenomenon (2) Trousseau's phenomenon may be produced by pressure over any nerve trunk If pressure is applied to the median nerve, the patient's fingers and hands assume a typical contraction with fingers folded about the thumb This position of the hands has been designated as the main d'accoucheur or obstetric position and is characteristic of tetany. (3) Schlesinger's sign or Pool's leg phenomenon is elicited in latent tetany by holding the leg at the knee and flexing strongly at the hip joint This maneuver is followed by extensor spasm at the knee joint with supination of the foot

The convulsions of tetany consist of tonic contractions of one or more muscle groups which last for a few minutes to several hours, during which there is intense pain The limbs and face are mostly affected, rarely the muscles of the abdomen, trunk, or neck. The feet may be extended Laryngospasm, due to spastic narrowing of the glottis, may produce a loud high-toned inspiratory noise

Hypocalcemia induces a prolongation of systole in the heart and can be recognized by an increase of the QT interval in the electrocardiogram

The bl [illegible]
hyperphos [illegible]
of serum. [illegible]
serum The [illegible]
100 ml

A low calcium content of the blood may be observed in some instances of rickets, osteomalacia, infantile tetany and renal insufficiency

The hyperphosphatemia of nephritis and uremia may be accompanied by hypocalcemia. This hypocalcemia is probably secondary to the increased phosphate content of the blood, which directly influences the state of the calcium. The removal of the protein-calcium-phosphate complex formed in the presence of excess phos-

tions which elevate this rate, such as febrile illnesses, cardiac failure, leukemia, lymphomas, and acromegaly, while in Addison's disease, cretinism, hypothyroidism secondary to panhypopituitarism, and in the presence of the nephrotic syndrome the metabolic rate will be abnormally low. Common causes too of aberrations in basal metabolic estimations are the escape of oxygen through a poorly fitting mouthpiece or through a punctured ear drum, entrance of other gases into the system, and depletion of the soda lime in the apparatus.

The basal metabolic rate is found to be in error in about one third of all of the determinations in the borderline cases as revealed by radioiodine studies. Approximately one half of these errors are found to be false high basal metabolism reading, and the other half are false normal or false low basal metabolism reading. In studies of comparisons of radioiodine studies with metabolic rates, values of more than +20 per cent are considered false high readings. If the basal metabolic rate is less than −20 per cent, this is considered a false normal or false low basal metabolism reading Once the true basal metabolic rate is known for an individual patient, the efficacy of treatment for hyperthyroidism and hypothyroidism can be gauged by *frequent determinations of the basal metabolic rate*

The clinical evidence for thyroid disease and the basal metabolism are still the basis for the diagnosis of these conditions except in the borderline cases.

THE PARATHYROID GLANDS

The parathyroid glands are four in number, each about 0 5 cm, in size. Normally they are situated one at each of the upper and the lower poles of the two lobes of the thyroid gland. However, they may be situated in other parts of the neck or in the anterior mediastinum

The only known function of the parathyroid glands is to produce and to release the *parathyroid hormone, a function performed without the aid of trophic hormones from* any other gland. The hormone regulates the excretion of inorganic phosphate in the urine.

If parathyroid hormone is administered to a patient who has no parathyroid glands, the *following sequence of events takes place.* (1) a marked excretion of urine containing an increased amount of phosphorus accompanied by a decrease in the concentration of the serum inorganic phosphorus, (2) an increase in resorption of calcium and phosphorus from bone which restores the phosphorus concentration of the serum to normal and increases the calcium concentration of the serum above normal limits The hypercalciuria is present because of the hypercalcemia The parathyroid hormone may exert its primary action directly on bone and cause its dissolution so that the serum electrolyte changes are secondary to the bone changes This is indicated by the observation that *parathyroid hyperplasia* occurs in conditions which produce a low serum calcium level (see Bone Diseases, Chapter 6).

Parathyroid hormone can be replaced in therapeutics by sterols such as dihydrotachysterol (A T 10) and calciferol (vitamin D_2) Both of these are irradiation products of ergosterol

The actions of calciferol and dihydrotachysterol resemble each other. Calciferol has a more definite effect on calcium absorption than on phosphorus diuresis Dihydro- [illegible] diuresis than to promote [illegible] dihydrotachysterol [illegible] with *calciferol is* due to increased absorption from the gastrointestinal tract Since the first action of dihydrotachysterol is on phosphorus excretion in the urine, *it much more closely* resembles parathyroid hormone than calciferol. It differs from parathyroid hormone in that it does cause some calcium absorption from the gastrointestinal *tract, whereas the* parathyroid hormone causes none. Since dihydrotachysterol induces hypercalcemia by mobilizing calcium from bone, it has no antirachitic action, whereas calciferol, which causes hypercalcemia chiefly by increasing absorption from the gastrointestinal tract, is antirachitic.

serum calcium. The serum calcium may reach concentrations of 15 or more mg per 100 ml. of serum. As a sequence of the increased concentrations of serum calcium larger quantities of calcium are excreted by the kidneys. The excess excretion of calcium leads to rarefaction of the bones or osteoporosis

In observing the sequence of the disturbance caused by an excess of parathyroid hormone it becomes obvious that the clinical manifestations may be attributable to. (1) a disturbance in the electrolyte equilibria which may become manifest before there are detectable changes in either the bones or disturbances in renal functional activity. When this sequence of events occurs the condition is termed the syndrome of hyperparathyroid intoxication (2) Excessive action of parathyroid hormone may be manifest by bone disease without quantitatively measurable disturbances in the electrolyte equilibria or renal functional activity or the presence of bilateral renal stones. This is a common form of the disease (3) Excessive parathyroid hormone may have renal stones as its sole or principal manifestation Commonly, however, there may be a combination of disturbances of electrolyte equilibria, bone changes and renal disease.

The pathologic changes in the parathyroids may consist of a generalized hypertrophy and hyperplasia—idiopathic hyperparathyroidism More commonly the pathologic condition consists of a single adenoma or multiple adenomas of one or more of the glands The adenomas have endocrine functional capacity They arise usually from the chief cells of the gland. However, occasionally an adenoma arises from either the transitional or the oxyphil cells. All adenomas are enclosed in normal gland tissue In rare instances a carcinoma will be present These carcinomas metastasize to the lymph nodes of the neck, to the shoulders and to more distant parts

The bone cysts occurring in hyperparathyroidism have no distinctive features Both giant cell tumors and bone cysts may be present in the same bone The cysts seem to represent quiescent bone lesions while the giant cell tumors represent activity Osteoporosis is eventually present to a degree in all the bones

Hyperparathyroidism is a rare disease which affects women more frequently than men Children may have the disease

Symptoms The symptoms are more conveniently discussed as they occur in association with the outstanding manifestations of the disease

The *syndrome of hyperparathyroid intoxication* may occur acutely, but never without evidence of a chronic illness indicative of hyperparathyroidism having been present for some time. It may be the first manifestation of osteitis fibrosa cystica or of renal stones or calcinosis. In any event the symptoms of hyperparathyroidism result from hypercalcemia and its ensuing injury consisting of increased excretion of calcium and phosphorus in the urine and skeletal changes The symptoms due to *hypercalcemia* are weakness, anorexia, nausea, vomiting, loss of weight, pains in muscles, joints and abdomen and incoordination, bradycardia and cardiac irregularities. Often there is a history of attacks of nausea and vomiting, polyuria and polydipsia, renal colic, constipation, and anemia Atonia of the muscles and hyperextensibility of the joints may be excessive Renal calcinosis may be an early symptom as the result of excessive calcium excretion in the urine. Hypercalcemia has occurred in those who are under treatment for peptic ulcer by a diet high in calcium and phosphorus

Parathyroid intoxication is manifested by fever, dehydration, nausea and vomiting, and mental confusion which proceeds to coma and death. This intoxication may also occur as an acute complication in chronic hyperparathyroidism.

Skeletal changes associated with osteitis fibrosa cystica (osteodystrophia fibrosa, parathyroid osteosis) consist of the process of generalized decalcification (osteoporosis), cysts and giant cell tumors, fractures, deformities and epulides The bones of the skull, the vertebrae, femora, radii, ulnae and pelvis are affected. There is thinning of the cortex and trabeculae of the long bones with cyst formation in the

anism whereby this occurs

ed if there is present in a young person numbness of the fingers, laryngeal stridor and convulsive seizures. If the young patient has mental retardation in addition to paresthesias, stridor and fits, the diagnosis is more strongly suspected. Acute hypoparathyroidism may occur after operations on the thyroid gland Paralysis of the vocal cords often is present too if there is hypoparathyroidism postoperatively, the recurrent laryngeal nerves having been injured at the same operation.

The criteria for the diagnosis of chronic hypoparathyroidism include the presence of tetany, a low serum calcium and an increased concentration of phosphate, the existence of normal bone texture, and the absence of renal insufficiency. Hypocalcemia also accompanies conditions of hypoproteinemia but in these tetany is not present.

Secondary Disturbances of the Parathyroid Glands. Enlargement of the parathyroid glands is not synonymous with idiopathic hyperparathyroidism (see below), for as a compensatory mechanism the parathyroids enlarge in osteomalacia, rickets, multiple myeloma, osteoporosis and osteitis fibrosa. All of these conditions are characterized by loss of calcium phosphate from the bones. In osteomalacia and rickets there is a faulty calcification of the skeleton due to vitamin deprivation In multiple myeloma the bone is destroyed by a malignant process

Basophilic adenomas of the hypophysis (Cushing's syndrome) and ovarian deficiencies are often accompanied by osteoporosis. The osteoporosis which occurs in the aged is referable to the cessation of reproductive activity The effects of pregnancy or lactation in aggravating latent tetany are due to the extra requirements which these conditions entail on the calcium supply of the organism

Administration of thyroid substance increases the calcium excretion through the intestine and results in a negative calcium balance without materially influencing the concentration of calcium in the blood

Deficiency of renal function stimulates hyperfunction and hyperplasia of the parathyroid glands, while hyperparathyroidism may produce renal lesions and renal failure. Certain renal diseases of long duration are accompanied by changes in the bones which resemble those due to parathyroid adenomas.

A failure of the kidneys to maintain a normal acid-base balance may induce osseous changes resembling those observed in osteitis fibrosa. Phosphate retention may affect the calcium-ion concentration of the blood and interfere with the absorption of calcium from the intestine As the result of renal disturbances the mechanisms of normal calcium and phosphate metabolism may affect the skeleton and give rise to osteodystrophy.

In both parathyroid insufficiency and vitamin D deficiency there may be a diminished calcium content of the blood, and there are changes in the skeletal system Hypertrophy of the parathyroids is observed only in low calcium rickets, and not in low phosphorus rickets Hypocalcemia rather than hyperphosphatemia is the primary cause of enlargement of the parathyroid glands in these conditions

Pseudohypoparathyroidism. Albright and his collaborators have reported instances of hypoparathyroidism in which there was evidence of failure of the organism to respond to the hormone. They suggested that the disturbance was not a lack of the hormone but a resistance to it

Hyp[illegible]

crease of the concentration of the serum phosphate (less than [illegible] 4 mg per 100 ml. of serum in infants) Because of the reciprocal relationship between serum calcium and serum phosphorus there is subsequent increase in the

serves as an aid in detecting suspected hyperparathyroidism before the typical skeletal changes have appeared.

Table 14-1. The Alterations in the Calcium, Phosphate and Phosphatase Observed in Several Common Disorders of the Bones

	Blood Serum Calcium	Blood Inorganic Phosphate	Alkaline Blood Phosphatase	Calcium Excretion in Urine
Hypoparathyroidism	Low	High	Normal	Low
Hyperparathyroidism	High	Low	High	High
Paget's disease	Normal	Normal	Very high	Normal
Osteomalacia	Low or normal	Low or normal	Increased	Low
Metastatic carcinoma of bone	May be high	May be low	May be high	High
Senile osteoporosis	Normal or slightly low	Normal	Normal	Normal
Multiple myeloma	High	Normal	Normal or slightly elevated	High

From Grollman, A, Essentials of Endocrinology, Ed 2, J B Lippincott Company, 1947.

In Table 14-1 are listed the changes in the blood and urinary calcium levels and in the blood phosphatase level seen in parathyroid and other common bone disorders.

Result of the Sulkowitch test for excessive calcium in the urine is positive If this test is performed, it is best to have the patient prepared by the Aub diet.

The inorganic phosphate concentration of the blood in hyperparathyroidism is usually reduced to 1.5 to 2.5 mg per 100 ml, compared with the normal concentration of 2 5 to 4 in adults, and 4 to 6 in infants and children The phosphatase level may be 20 units or more, compared with the normal level of 1.5 to 4 units.

DIAGNOSIS The diagnosis of hyperparathyroidism is based on the concentrations of the calcium and phosphorus in the blood, provided the diseases resembling hyperparathyroidism such as adolescent rickets, osteomalacia, senile osteoporosis, extensive metastatic carcinoma, multiple myeloma, Paget's disease, and polyostotic fibrous dysplasia are excluded Some of these disorders, however, can be differentiated by chemical examination of the blood (see Table 14-1). The rest can be differentiated by roentgenograms and clinical manifestations In polyostotic fibrous dysplasia the bone cysts resemble those seen in hypoparathyroidism, but the lesions in this condition are unilateral and the osteoporosis is limited to the region surrounding the lesion. In hyperparathyroidism there is usually generalized rarefaction of the cortex of the bones Hyperparathyroidism may occur without marked decalcification, the presenting symptoms being renal lithiasis or an anemia

The generalized decalcification of the bones, the hypercalcemia and the spontaneous fractures seen in multiple myeloma may suggest hyperparathyroidism However, the presence of Bence Jones protein in the urine (in about two thirds of the patients), the absence of hypophosphatemia, the hyperproteinemia of the blood, a biopsy, and the roentgenologic appearance of the bones will delineate multiple myeloma in most instances.

In metastatic carcinoma of the bone increased values for calcium and phosphatase in the blood and the presence of localized regions of osteoporosis may suggest hyperparathyroidism. In carcinoma the decalcification is irregular, and a primary lesion in a breast, a kidney or the prostate may be obvious If such a lesion is not obvious, the rapid failure of health soon will permit of a definite diagnosis

center of the shaft Owing to softening of the skeleton, devastating deformities result from gradual collapse of the spinal column, pelvis and thoracic cage (see Bone Diseases in Chapter 6).

The osseous changes in the disease result in deformities of the skeleton, and multiple fractures occur spontaneously or as a result of minor injuries The disease is commonest in middle life. It begins with generalized weakness, excessive thirst and frequent urination Pains in the back, pelvis and legs develop so that locomotion may become difficult or impossible. The skull is enlarged, the spinal column shortened and kyphotic Irregular deformities of the extremities appear. Atonia and general muscular weakness develop

The symptoms of osteitis fibrosa cystica are referable mainly to the locomotor system and comprise muscular weakness and bone pains. Sharp pain may follow slight trauma Later it is discovered that a pathologic fracture has occurred Deep pains in the heels, legs, and hips, and extending upward to the lumbar portion of the spinal column, are present after exercise and seemingly are worse after retiring for the night. The patient may observe that his stature has changed The body height lessens and there is excessive bulging of the breast bone Owing to a shortened, thickened neck, a larger collar may be necessary Pains in the shoulders, arms and hands may be present alone or may accompany those of back, legs and feet.

Often there is the history of having had a bone tumor diagnosed as a cyst by the surgeon After removal of the cyst the bone pains continue

Urinary lithiasis is frequent in those who have hyperparathyroidism However, only a fraction of the patients who present themselves with renal stones are found to be suffering from hyperparathyroidism In all cases of bilateral urinary lithiasis the possible existence of hyperparathyroidism as the causative agent is considered Polyuria, polydipsia, dysuria, albuminuria and hematuria are frequently present. In long-standing hyperparathyroidism, nephrocalcinosis may result and death may occur from renal insufficiency The deposition of calcium in the kidneys is usually interstitial with secondary obstruction of the tubules

EXAMINATION The parathyroid tumors, one or more, which are responsible for hyperparathyroidism are rarely palpable Frequently they are imbedded in the thyroid gland or present in the mediastinum

Examination of the mouth and the jaws reveals epulides or other soft-tissue tumors of the gums and the jaw There may be malocclusion and distortion of the normal arrangement of the teeth with prognathism of the mandible

On examination of the bones usually no gross abnormalities are present A fracture may be the occasion for the examination, and the nature of the fracture is revealed on roentgenologic examination In the jaws the roentgenograms reveal cystlike cavities, presence of dental caries, osteoporosis, closely meshed trabeculae of the mandible and maxilla and absence of the lamina dura of the teeth The bone cysts which are observed in patients suffering from hyperparathyroidism resemble ordinary solitary benign cysts seen in other conditions

Hyperparathyroidism is almost always associated with an increase of the concentration of calcium in the blood to 12 mg per 100 ml or more Values of more than 20 mg. have been reported in parathyroid intoxication Occasionally, however, the blood calcium concentration is within normal limits, but this occurs only if the serum protein level is abnormally low, or if there is phosphate retention due to secondary renal insufficiency Under these conditions there is actually an effective hypercalcemia despite the apparently normal concentration of the total calcium.

Normally about 70 to 95 per cent of the total calcium ingested is excreted in the feces, only a small amount appearing in the urine In hyperparathyroidism as much as 70 to 90 per cent of the ingested calcium may appear in the urine The total calcium excreted is increased so that there is a negative calcium balance The existence of this negative calcium balance in patients maintained on a low calcium diet

neogenesis) is enhanced. This conversion of amino-acid radicals to dextrose is anti-anabolic, but it is not catabolic. Cortisone increases the mobilization and utilization of fat, thereby sparing carbohydrate There is a diminished oxidation of the available carbohydrate. The sum total of the foregoing mechanisms results in an increase in the concentration of blood sugar.

Cortisone has an action on sodium and potassium metabolism which is quantitatively about 3 per cent of that of desoxycorticosterone The mechanism of action of the two is different, however; and when they are given together in certain relative dosages, they may tend to neutralize each other in electrolyte effect

Cortisone also causes lysis of lymphoid tissue, with diminution in size of the lymph nodes and the thymus. It produces a lymphocytopenia, a sharp drop in eosinophil count, and a neutrophilic leukocytosis which is usually sufficient to cause a slight increase in the total white blood cell count. The steroid also increases the renal excretion of uric acid.

The gluco-corticoids play an important part in meeting certain types of stress, such as infection, trauma (including burns), solar and roentgen irradiation, intoxications of various sorts, extremes of temperature, excessive exertion, strong emotion, malnutrition, and the effects of some drugs.

The ability of the 11, 17-oxycorticoids to counteract the effects of damaging agents is strikingly shown in the results of administration of cortisone and of ACTH in rheumatoid arthritis, rheumatic fever, gout, lupus erythematosus, and other diseases In rheumatoid arthritis, for instance, the daily injection of 100 mg or more of cortisone acetate is followed within a few days by reduction of stiffness, diminution in articular tenderness and pain on motion, reduction of swelling, and great improvement in articular and muscular function; improved appetite and gain in weight, increase in feeling of well-being sometimes amounting to euphoria, great reduction (sometimes to normal) in blood sedimentation rate; improvement in anemia, and return toward normal in plasma protein level and distribution. However, the effects seldom outlast the period of administration.

Large doses of cortisone (of the order of 100 mg daily) are capable of producing Cushing's syndrome. If administration of the drug is stopped promptly, the manifestations cease Similar doses have also induced psychoses of various types, some of which have persisted after withdrawal of medication Diabetes mellitus has also been precipitated in susceptible individuals

Lipocorticoid. The compounds, such as 11-dehydrocorticosterone (compound A of Kendall), probably influence the metabolism of fat Although some clinical and experimental evidence indicates that the adrenal cortex is involved in the metabolism of fat, this is one of the least explored aspects of the function of the adrenal cortex. Obesity is one of the outstanding features of some patients who have hyperfunctioning lesions of the adrenal cortex On the contrary, patients who have Addison's disease have difficulty in gaining weight. Thorn has observed a decrease in the fecal excretion of fat by patients with Addison's disease who are treated with compound A Some evidence indicates that these compounds are a part of the group of hormones, the urinary excretion products of which are measured collectively as the so-called glycogenic corticoids or corticosteroids

Figuratively speaking, in times of stress epinephrine and norepinephrine prepare the body for fight or flight, whichever the cerebral cortex decides is expedient in the given situation and circumstances However, if the stress is prolonged or if the body constituents are damaged, the cortical hormones function to produce, or aid in the production of, resistance to the damaging influences. Cortical hormones tend to hold in check tissue reaction to damage

Exposure to cold, heat, burns or trauma, prolonged muscular activity, fasting, chemical and bacterial agents, or disease processes cause at first an increase in the production of cortical hormones, followed by hypertrophy and increased activity of the adrenal cortex These hormones assure an adequate production and supply of blood glucose, even at the expense of the body protein causing a negative nitrogen balance if the need for glucose is great enough. Increased production of adreno-

THE ADRENAL GLANDS

Cross section of an adrenal gland reveals the two component parts, an external (or cortical) and an internal (or medullary) portion. The gland elaborates certain androgens from its cortex and epinephrine from its medulla.

ADRENOCORTICAL HORMONES. Adrenocortical hormones are grouped chemically under the term steroids The fundamental organic chemical ring system of the sterols, bile acids, sex hormones and adrenal hormones is the perhydrocyclopentenophenanthrene ring system which has a system of identification of its compounds unlike other organic ring systems.

All of the adrenocortical steroids that have been isolated are derivatives of pregnane Progesterone and estrone have been isolated from adrenal extracts but they are also ovarian products Androgenic substances with the same number of carbon atoms as androsterone also have been isolated from adrenal extracts Many compounds have been isolated from cortical extracts of the adrenal glands. However, here brief description will be given of only the commoner ones.

Mineralo-corticoids The steroids which have as their predominant action an influence on sodium and potassium metabolism are 11-desoxycorticosterone (desoxycorticosterone) and 11-desoxy-17-hydroxycorticosterone (Reichstein's Compound S)

The mineralo-corticoids cause retention of sodium and elimination of potassium. Most of this effect is exerted through the kidneys, in which these steroids act specifically on the cells of the proximal convoluted tubules to stimulate reabsorption of sodium, chloride and water are reabsorbed secondarily, and there is an increase in volume of the plasma and interstitial fluid. The renal excretion of potassium is increased, but the mechanism is not understood In addition, the mineralo-corticoids influence capillary permeability and tissue affinity for electrolytes and water These actions are associated with a decreased concentration of sodium and chloride in the sweat Both the mineralo-corticoids and the gluco-corticoids exert slight androgenic and progestational effects.

Desoxycorticosterone is the most potent. It is made synthetically and occurs in the adrenal cortex in minute quantities only, if at all It is the only mineralo-corticoid now generally available.

Desoxycorticosterone acetate (DCA, Doca, Cortate, Percorten) is employed clinically in the treatment of Addison's disease It is usually injected intramuscularly in oil solution The average dose is 2 to 3 mg daily, but in every case the dosage must be individualized to meet the needs of the patient at the time After the drug has been given for a considerable period and the requirement has been thoroughly established, pellets may be implanted in those patients whose requirements show little fluctuation

Patients receiving desoxycorticosterone should have a definite intake of sodium, which may be in the form of the chloride, bicarbonate, or citrate The usual intake is 3 to 5 gm. in addition to that needed to season the food Increasing the dose of sodium salts diminishes the requirement of hormone, and vice versa Patients receiving hormonal therapy should also take up to 2 gm of potassium daily in the diet to prevent potassium deficiency.

Hypopotassemia may cause replacement of tissue potassium with sodium, the result is muscular weakness or paralysis Prolonged overdosage may induce degenerative changes in the arteries, including nephrosclerosis These manifestations are rare if patients receive the minimal effective dosage (2 gm daily)

Desoxycorticosterone has no effect on carbohydrate metabolism, it is especially important that patients who have Addison's disease and who are receiving desoxycorticosterone have a high carbohydrate intake There should be frequent feedings, including one at bedtime.

Gluco-corticoids. The two best known gluco-corticoids are corticosterone and cortisone. Being the most readily available of the gluco-corticoids, cortisone is discussed as typical of the group

Cortisone (Kendall's Compound E) effects increase in conversion of exogenous carbohydrate to glycogen. The conversion of endogenous protein to carbohydrate (gluco-

of the tubercle bacilli Extensive tuberculous destruction of both adrenals may be encountered with comparatively little tuberculosis in other organs.

In one fourth of those who have Addison's disease there is primary atrophy of the glands or an amyloid disease. The attributable causes of secondary atrophy of the glands are neoplasms, fatty degeneration, pressure atrophy, venous thrombosis, arterial embolism and syphilis.

Characteristic findings, other than those observed in the adrenal glands, are extreme emaciation, small and atrophic heart, hypoplasia of the aorta and large vessels, atrophy of the mucosa, enlarged lymphoid follicles of the stomach and intestines, persistent thymus, and often enlargement of the spleen Renal tubular atrophy may account for the renal dysfunction responsible for the disturbance in the water-and-salt metabolism observed in the disease. The gonads may show atrophic changes

SYMPTOMS. Fatigue is the early symptom The patient becomes incapable of physical or mental effort. The patient is often apathetic and subject to depression, and irritability is increased Headaches, tinnitus, vertigo and insomnia, and pains in the lumbar region, epigastrium, and extremities are common Anorexia, nausea, and constipation alternating with diarrhea may begin early and recur with increasing frequency and severity. Thus asthenia, gastrointestinal disturbances and pigmentation constitute the cardinal symptoms of Addison's disease. Loss of weight and abdominal or lumbar pain are also common complaints

The so-called crises are common In an acute crisis the gastrointestinal disturbances such as nausea, vomiting, diarrhea, and abdominal pains may be severe.

Loss of weight is due to dehydration secondary to excessive loss of sodium, chloride and water, and impaired gastrointestinal function with anorexia and inanition

Characteristic of Addison's disease is the occurrence of spontaneous remissions. Patients who have the disease may live for 10 to 20 years without treatment after the onset of the initial symptoms

EXAMINATION. The pigmentary abnormalities of the skin are an increased pigmentation, and in some a complete loss of cutaneous pigment (vitiligo) in areas or spots Excessive tanning following exposure to the sun with a persistence of the sun tan is frequently observed Dark-skinned persons with a given degree of adrenal insufficiency will show much more pigmentation than those who have blond skin. Increase in pigmentation is common in the anogenital region and in the areolae about the nipples; in scars; over the knees, elbows, and buttocks, in brown to bluish black areas on the lips, gums, and ocular fundi, and on the buccal, rectal and vaginal surfaces The hair darkens The pigment changes in the skin may be absent throughout the course of the disease

Reduction in blood pressure is present in all patients who have Addison's disease It is to be recalled that many normal persons have systolic blood pressures between 90 and 100, measured in millimeters of mercury. Profound hypotension develops late in the course of the disease A patient who has an existing hypertension at the time of onset may exhibit all of the clinical signs of advanced Addison's disease and yet present a normal blood pressure. The heart characteristically is small

Addison's disease is accompanied by a moderate neutropenia, lymphocytosis, and an eosinophil count varying from high normal upward. After excessive loss of sodium, chloride and water, the levels of sodium and chloride tend to be low with an increased serum potassium and nonprotein nitrogen.

In severe Addison's disease, hypoglycemia is observed.

Patients who have Addison's disease are extremely sensitive to insulin, and severe reactions may be induced by the administration of quantities as small as 3 to 5 units

The secondary sex characteristics are not specifically affected by adrenal cortical insufficiency. The menstrual cycle and gonadal functions are maintained.

cortical hormones, if sustained, causes atrophy of the thymus and of other lymphoid tissues. The polymorohonuclear count is increased and the lymphocytes and eosinophils are decre[illegible] of uric acid is increased in the blood and urine

The response of t[illegible] through the pituitary gland by [illegible] The cerebral cortex, the adrenal medulla, [illegible] form a closely knitted unit in the protection of the individual [illegible] in the repair of injury sustained from trauma or infection

The response of the body tissues to epinephrine is mediated through the sympathetic nervous system, the stimuli having reached the cortex through the sense organs.

Adrenal Insufficiency (Hypofunction of Adrenal Cortex) Adrenal cortical insufficiency occurs in both acute and chronic forms.

Acute Cortical Adrenal Insufficiency. Acute collapse associated with bilateral adrenal hemorrhages may occur in the newborn, and is characterized by fever, tachypnea, cyanosis and convulsions. The condition is often associated with difficult prolonged labor which requires manipulation or instrumentation in order to accomplish delivery

The Waterhouse-Friderichsen Syndrome The Waterhouse-Friderichsen syndrome occurs in overwhelming sepsis, resulting as a rule from meningococcal infection, but may occur in a variety of other fulminating septicemias also There are dehydration, purpura, shock, a decrease in serum sodium, and an increase in the nonprotein nitrogen At necropsy the adrenal glands are hemorrhagic

In children and adults alike the insufficiency occurs most frequently in association with severe infections such as staphylococcal septicemia, meningococcemia, influenza, and streptococcal infections There is almost always an associated generalized hemorrhagic manifestation

Shortly after the onset there is a generalized cyanosis It is soon followed by a rash, which is petechial at first, but may soon become blotchy and confluent over the whole body The rash, characteristically, does not fade on pressure Fever at first is moderate but it becomes extreme Temperatures of 107 to 108 F (41 7 to 42 2 C) may be reached prior to death As in sunstroke, brain tumors and other conditions associated with such high fevers, symptoms due to the central nervous system such as stiffness of the neck, increased irritability, and finally convulsions, stupor, coma and death quickly ensue In other cases the temperature may fall, the pulse becomes weak and thready, the blood pressure may become unobtainable, and the patient dies in shock In most instances the entire course of events occurs in 12 to 24 hours

Laboratory studies usually reveal a marked polymorphonuclear leukocytosis with normal eosinophil counts Hypoglycemia is severe There may be an increase of nonprotein nitrogen concentration of the blood The concentrations of serum sodium and potassium are within normal limits

Acute adrenal cortical insufficiency which may follow operative procedures on the adrenal glands may be anticipated and therapy tried

Addison's Disease (*Chronic Cortical Adrenal Insufficiency*). Addison's disease is a rare disease which is due to a chronic adrenal cortical insufficiency. It occurs usually in men between the ages of 20 and 40 years, but it may be encountered at any age. The patients usually live long enough to visit several institutions and thus to be recorded several times.

In half of the patients who have Addison's disease the destructive process of the adrenal glands is tuberculosis.

The tuberculous lesion of the adrenal glands is originated by hematogenous spread

voided during any one of the one-hour periods of the morning (that is, of the specimens collected at 9:30, 10.30, 11:30 and 12:30), the patient presumably does not have Addison's disease. If the volume of the night urine exceeds that of any single morning specimen, further chemical studies are indicated The urea and chloride contents of the night urine and of the blood plasma are determined These values expressed in the same units are then substituted in the following equation

$$A = \frac{\text{urea in night urine}}{\text{urea in plasma}} \times \frac{\text{chloride in plasma}}{\text{chloride in night urine}} \times \frac{\text{volume of day urine}}{\text{volume of night urine}}$$

If A is 25 or less, the patient probably has Addison's disease, if A is 30 or more, the disease is not likely to be present.

This procedure is not specific for in patients who have asthenia and exhaustion not of adrenal origin false positive results may be obtained

DIAGNOSIS. The presence of pigmentation, asthenia, hypotension, and gastric disturbances is suggestive of Addison's disease In instances in which the diagnosis is not certain some one, or all, of the special tests described, such as the salt deprivation test, may be employed Pigmentation similar to that which occurs in Addison's disease is most commonly observed in individuals of mixed races, dark-skinned and white-skinned. Sometimes in pregnancy, uterine disease, hemochromatosis, chronic arsenic poisoning, pernicious anemia, ochronosis and Recklinghausen's disease the distribution of pigmentation may resemble that present in Addison's disease. Asthenia and hypotension are accompaniments of most protracted debilitating illnesses, as are also digestive disturbances. Pernicious anemia and abdominal tuberculosis may show a superficial resemblance to Addison's disease

Hyperfunction of the Adrenal Cortex. The adrenal cortex may begin to function excessively without any demonstrable histologic changes in its structure. In some there may be present a cellular hyperplasia, in others overactivity can be accounted for on the basis of a benign or malignant tumor if the tumor cells secrete cortical hormones. However, either benign or malignant tumors may be present without glandular hyperfunction

After protracted infections *simple hyperplasia* of the adrenal glands frequently is observed. Cortical hyperplasia is considered to be simple hypertrophy in response to an increased demand on the part of the organism.

The syndromes of hyperfunction of the adrenal cortex are extremely protean in nature and presumably depend on the type and quantity of steroid hormones produced, the age and sex of the patient, and perhaps on other factors Anyway, these syndromes may defy the ability of the expert to separate them. The syndromes may be divided into two large categories as follows: (1) Cushing's syndrome and (2) the adrenogenital syndrome

Cushing's Snydrome (*Adrenal Cortical Hyperfunction*). The Cushing syndrome, believed by Cushing to be caused by a basophilic adenoma of the pituitary body, is now generally regarded as being associated with hyperplasia of the adrenal cortex or tumors of this tissue.

In a few of the cases there is a basophilic tumor. Occasionally the basophilic tumor has eroded the sella turcica In isolated instances there may be a chromophobe tumor or a mixed tumor. When a tumor is present the syndrome is then designated Cushing's disease

In adrenal cortical hyperfunction many different combinations of manifestations are possible and it is for this reason that so much has been written about the Cushing syndrome. An overproduction of the mineralo-corticoids may result in hypertension, edema, decreased concentrations of plasma potassium (less than 15 mg per 100 ml.) and occasionally increase in sodium (more than 350 mg. per 100

Sclerotic changes in the pinnas of the ears may be present in long-standing ison's disease.

In Addison's disease there is a reduced 17-ketosteroid excretion. However, : 17-ketosteroids are found to be decreased in the presence of wasting disease, w 17-ketosteroid excretion is not pathognomonic.

A number of tests have been advocated for aids in diagnosis if the findings on ical and laboratory examinations are inconclusive

The Response to Pituitary Adrenocorticotropic Hormone A test for adrenal cortical ficiency based on the failure of patients who have Addison's disease to secrete cal hormones in response to the pituitary adrenocorticotropic hormone has been loped by Thorn, Forsham, Prunty and Hills

The maximal fall in circulating eosinophils and the maximal increase in excretion of acid occur approximately four hours after the intramuscular injection of the ione Patients who have classic Addison's disease fail to show these changes after nistration of the hormone.

The 48-Hour ACTH Test This is the most reliable of the tests based on the response e normal adrenal cortex to its trophic hormone as described by Thorn and co-ers Twenty-five or more milligrams of ACTH is given intramuscularly or intra-usly at 6-hour intervals for a 2-day period. The excretion of 17-ketosteroids during econd 24-hour period during the administration of ACTH and the number of cir-ing eosinophils are compared to values obtained prior to the administration of H A rise of less than 3 or 4 mg in the 17-ketosteroid excretion in the urine accom-d by less than 40 to 50 per cent decrease in circulating eosinophils is indicative of ial cortical insufficiency

The Response of the Circulating Eosinophils to Administration of ACTH The normal s of the 17-ketosteroids for adult men between the ages of 20 and 40 years range 10 to 20 mg per 24-hour urine specimen, the normal female value for the same roup is from 8 to 15 mg In both boys and girls there is less than 1 mg per day at and concentrations between 1 and 2 mg. until the age of 8 years, thenceforward is a gradual increase until adult concentrations are attained In aging men and en there is a gradual decrease in the concentration of the 17-ketosteroids in the urine . low 17-ketosteroid concentration in the urine is compatible with the diagnosis of son's disease but not pathognomonic of it In hypopituitarism the concentration of tosteroid is very much decreased Also, low concentrations of 17-ketosteroid in rine may occur in chronic disease of various origins, as well as being decreased in resence of both hypothyroidism and hyperthyroidism

The concentration of the 11-oxysteroids is greatly decreased in both primary and dary adrenal cortical insufficiency The determination of the urinary 17-ketosteroids, ugh a less specific index of cortical activity, is more easily carried out and entirely actory for clinical purposes In women the adrenal cortex is the only important e of these compounds or their precursors, where in men the testes make additional ibution it is for this reason that 17-ketosteroid excretion is normally 50 per cent er in men than in women

Sodium Restriction Test Kepler, Robinson and Power described what is considered a *safe sodium restriction test* to supplant the test advocated by Cutler, Power and er This test may be performed if need be for diagnostic purposes In the so-called test the patient eats three ordinary meals on the day preceding the test, without g any extra salt. Nothing is eaten or drunk after 6 P.M on the day of the test At) P.M the bladder is emptied and the urine discarded At 7.30 the following morn-ne urine is collected, measured and set aside for analysis, if subsequently required. .30 A.M. the patient voids again This urine is discarded and 20 ml of water per ram of body weight (9 ml. per pound) is administered orally during the next 45 tes. The patient voids hourly at 9 30, 10.30, 11·30 A M. and 12 30 P M and each men is measured. The patient should remain at rest in bed throughout the period of est While the patient is fasting, blood samples are drawn for determinations of and chloride

The findings in the test just described are interpreted as follows: If the volume of : urine (that is, of the specimen collected at 7:30 A.M) is less than the volume

to the formation of renal calculi. Concentrations of the plasma calcium, phosphorus and phosphatase are within the normal limits.

Hypertension when present is usually grouped as benign. However, malignant hypertension with associated retinitis, edema of the optic disks, cardiac enlargement, heart failure and cerebrovascular accidents may occur and if so usually persist after the removal of the tumor.

There may be polycythemia, lymphopenia, and eosinopenia of varying degrees.

Diabetes often is present. An insulin resistant type of diabetes may be the only evidence of an adrenocortical tumor.

The concentration of the plasma potassium may be reduced and occasionally there is present hypochloremic alkalosis with or without an increased concentration of plasma sodium. The urinary 17-ketosteroids are usually normal in amount, but may be increased Bio-assay or chemical analysis of the urine for cortin-like substances usually reveals increased values

The patient who has Cushing's syndrome is not being injured by an excess of androgens and for this reason concentration of the 17-ketosteroids may be within the limits of normal. When Cushing's syndrome is due to bilateral adrenal hyperplasia, the concentration of the 17-ketosteroids in the urine is only slightly increased When Cushing's syndrome is caused by adrenal cortical adenoma the concentration of the 17-ketosteroids in the urine may be depressed; whereas in a patient who has adrenal cortical carcinoma, the 17-ketosteroid concentration in the urine is greatly increased. Decreased concentration of the 17-ketosteroids in the urine in the presence of adrenal cortical adenoma seems to be accounted for by the presence of atrophy of the contralateral adrenal gland

DIAGNOSIS The diagnosis when classic manifestations of Cushing's syndrome are present seems to be made frequently These manifestations are obesity (moon face), shrunken weak legs and arms, thin skin, hypertension, virilism, diabetes, osteoporosis and an increase in the excretion of 17-ketosteroids. The definite diagnosis of the varying degrees or syndromes which may be present in cortical hyperplasia and in tumor is difficult The isolation of dehydroisoandrosterone or the finding of a high ratio of the beta to the alpha ketosteroids is evidence of the presence of an adrenal tumor The excretion of pregnanediol may be increased: 30 mg. daily in cases of hyperplasia of the adrenal, compared with 5 to 10 mg. at the peak of the normal menstrual cycle In the absence of pregnancy this is significant.

Roentgenograms of the sella turcica should be made to rule out Cushing's disease. Negative roentgenograms of the kidneys and suprarenal areas will help to eliminate the possibility of adrenal tumor

The Adrenogenital Syndrome. The term adrenogenital syndrome is applied to cases of hyperadrenocorticism in which there is usually excessive masculinization attended by rapid growth, particularly in height, muscular development and accelerated epiphysial ossification Here there seems to be an increased protein anabolism due to excessive production of androgen, whereas in the Cushing syndrome there seems to be an increase of the glycogenetic hormone causing amino acids to be utilized for the formation of carbohydrate rather than building of protein tissues. Masculine hirsutism is present in both the adrenogenital and the Cushing syndrome

The adrenal cortical extracts contain estrogens, androgens, progesterone-like substances and cortilactin which acts on the breasts Despite the presence of these substances in cortical extracts there is no proof that the adrenal cortex is normally concerned with the regulation of sexual functions In disease excessive amounts of one or more of the sex hormones may be present in the adrenal cortex with consequent derangement of sexual function.

As in Cushing's syndrome the changes in the adrenal cortex in the adreno-

ml.) of the plasma. An increase of 11-dehydro-17-hydroxycorticosterone causes a wasting of the bone (osteoporosis) and muscles; lymphopenia, eosinopenia, a thin skin, ecchymosis and in some cases diabetes mellitus. In women there are amenorrhea, hirsutism and increased vigor.

In all instances there are changes in the cortical tissue of the adrenal glands consisting of a benign hyperplasia or neoplasm either benign or malignant.

In the pituitary body there are cytoplasmic hyalinization of the basophilic cells, disappearance of the basophilic granules, excessive vacuolization, ballooning of the nuclei, and general enlargement of the cells

Gross and often severe disease of the pancreas frequently is present. Infiltration of the liver with fat, and chronic passive hepatic congestion are noted frequently. There is a high incidence of nephrosclerosis, renal calcinosis and renal calculi The incidence of the presence of renal calcinosis with formation of calculi is an expected accompaniment of the osteoporosis and the calciuria. Hypertrophy of the heart is frequent Occasionally infiltration of the parathyroid bodies with fat is observed.

SYMPTOMS. Cushing's syndrome is uncommon in children. It commonly occurs in young women but may affect boys or men. The symptoms may arise from any one of the many manifestations of the disease The disease may have begun and progressed slowly so that the young woman comes to the physician because of disgust with her hairy fat face, feelings of tension in the head and nosebleeds In others the increased deposits of fat around the neck and face may have become painful There may be symptoms of hypertension, diabetes or deep aching pains of the bones arising from the osteoporosis. The flesh may bruise easily, the skin is thin and bleeds excessively from shallow cuts or abrasions

A wide variety of mental symptoms may be present These range from mild reactive depressions to severe and profound depressed states. Severe mental disorders may be present in patients who have Cushing's syndrome.

EXAMINATION On examination usually there is a pad of fat over the lower cervical and upper thoracic regions of the back The upper lids and the corners of the mouth droop The cheeks are florid, full, and large enough to obscure the ears when the face is viewed from the front (the so-called moon face). In children the neck may be obscured by drooping fat cheeks. The fat cheeks extend forward and sag enough so that the mouth appears small and deeply set in the face There are wasting and weakness of the muscles combined with obesity in which there is an abnormal distribution of fat, the combination of which makes the trunk, face and neck appear obese and the extremities thin. Extreme obesity is not commonly observed in Cushing's syndrome except when the disease occurs in childhood.

There are muscular weakness and atrophy in the legs. There is a relationship of the muscular weakness and the concentration of the plasma potassium. The potassium is decreased.

The skin is so thin that the superficial veins are made evident by their contrasting bluish color. All degrees of acne may be present, including acne pustulosa and acne indurata. The acne is made more evident by red thin skin (androgenic flush).

The skin over the lower part of the abdomen, the anterior lateral aspect of the thighs, the upper part of the arms, the axillae, pectoral regions and breasts is striped with purplish parallel linear striations These striae develop rapidly and may become ecchymotic, infected and necrotic.

There are hirsutism, hypertension, osteoporosis, diabetes, either latent or manifest, ecchymoses, and amenorrhea or impotence. Except for the presence of hirsutism, there is little or no evidence of masculinization

The osteoporosis of Cushing's syndrome as described by the roentgenologist is present in the vertebral column, the skull, the ribs and other bones. Compression fractures of the spinal column may occur. Hypercalciuria, when present, may lead

Precocious puberty is often one of the initial symptoms which induce the parents of children who have hyperfunctioning adrenocortical lesions to consult a physician Among afflicted girls the puberty proceeds along masculine lines. Hair appears on the pubes, the extremities and the face, the clitoris enlarges, the larynx enlarges and the voice deepens, and in cases of long standing the musculature, the skeletal framework and the distribution of subcutaneous fat all become masculine in type. In some cases of adrenocortical tumor puberty seems to be dissociated so that it proceeds along both masculine and feminine lines with masculine traits predominating. However, in some there is a mixture of masculine and feminine characteristics, including vaginal bleeding and development of the breasts A pure homologous sexual precocity does not occur in the female sex as the result of adrenal cortical hyperfunction Homologous sexual precocity in the female is due either to a granulosa cell tumor of the ovary or to one or several intracranial lesions (internal hydrocephalus, and tumors of the hypothalamus, pineal body or contiguous structures).

In girls there are hypertrophy of the labia majora, projection of the labia minora and enlargement of the clitoris, which may resemble a penis in structure In boys, in whom the disease is infrequent, there are excessive muscular development, deepening of the voice and hirsutism. There is enlargement of the penis, but the testes remain immature. There is usually a luxuriant growth of the pubic and sometimes of the facial hair, giving the impression of maturity

In the adrenogenital syndrome there is no true precocious puberty as observed in tumors of the testes and ovaries and in the pineal and hypothalamic disorders. There is neither menstruation nor spermatogenesis as observed in true precocious puberty.

On examination if there is a single meatus situated between the labial folds it should be determined whether this is a urogenital sinus or a normal urethra. This is determined by passage of a urethroscope with skilled hands In some instances the communication is delineated by means of roentgenograms In still other instances when physical examinations are impossible it may be well to ask the surgeon to explore and biopsy the gonads to determine their histologic structure The surgeon who performs an exploratory operation on such a patient is acquainted with the different abnormal embryonic developments which attend, congenital adrenal hyperplasia in females, the hermaphrodites (intersexes), the pseudohermaphrodites (male and female)

The congenital hormonal reversal in the female or those reversals occurring after birth are attended by masculinizing characteristics, increased bone growth and excessive excretion of 17-ketosteroids

The Adult Form (Adrenal Virilism). In the adult the adrenogenital syndrome almost always occurs in girls during the latter years of adolescence or in women at the time of the menopause

Virilism may occur in women who have (1) adrenal cortical hyperfunction, (2) arrhenoblastomas of the ovaries and (3) after prolonged administration of testosterone. Arrhenoblastomas manifest none of the distinctive features of the adrenogenital syndrome or distinctive metabolic features The administration of testosterone is determined by the history

In adrenal virilism, hirsutism may be the most annoying manifestation to the patient Hirsutism without virilism is usually hereditary in origin. Likewise hirsutism, obesity and oligomenorrhea without other symptoms of virilism are rarely attributable to adrenal cortical hyperfunction

Women who have hirsutism, mild virilism including muscular strength, and sterility usually enjoy environmental adjustment and make good wives.

In the adult form of the adrenogenital syndrome there is a retrogression of the

genital syndrome are variable. There may be no detectable anatomic changes or hyperplasia or a tumor. Tumors of the adrenals accompanied by changes in the reproductive system and somatic type indicative of sexual reversal are more frequent in the female than in the male.

As in Cushing's syndrome the manifestations depend on the sex and the age of the patient at the time of the inception of the disorder. The adrenogenital syndrome, therefore, can be classified into the female pseudohermaphroditic and the juvenile types, as it occurs in children before puberty; the adult type, which gives rise to virilism in adolescent girls and women

The Female Pseudohermaphroditic Type (Adrenal Virilism). The pseudohermaphroditism as it occurs in congenital adrenal hyperplasia is the commonest adrenal cortical disorder encountered during childhood. The condition is characterized by prenatal abnormalities of the sex organs which are followed by an excessive production of androgen thereafter.

The prenatal abnormality consists of a persistent genital duct in the female which forms a urogenital sinus as in the male The vulva is but a shallow groove between hypertrophied labia majora. The labia minora are rudimentary The clitoris, by the time of birth, is hypertrophied

Due to the excessive secretion of androgen, growth, muscular development and epiphysial ossification advance more rapidly than in the normal.

Some infants may have normally formed genitals but have an excess of cortical hormones at birth The manifestations of excess of cortical hormones at birth are divisible into (1) those who develop an adrenogenital syndrome early in life which may be followed by the development of Addison's disease; (2) those who have manifestations of Addison's disease at birth and usually die soon thereafter. Symptomatically the infants of the latter group resemble those whose condition arises from atresia of the duodenum or atresia in the proximal portion of the small intestine

Virilism and pseudohermaphroditism may affect either sex. Feminine pseudohermaphroditism is most often associated with adrenocortical hyperplasia and is rarely found in cases of adrenocortical tumor

In pseudomasculine hermaphroditism there are secondary male characters with female generative organs. The male characters may be the result of an androgenic activity of the adrenal glands which may be a part of the congenital maldevelopment If this be the case, these glands exert their androgenic influences early in embryonic life, for it is only at this time that the observed relationships of the organs could have assumed their abnormal forms

From birth on, these infants show evidences of increased secretion of androgen. Somatic growth, muscular development and epiphysial ossification become far advanced for the age of the patient. Frequently pubic and axillary hair and acne appear by the age of 2 to 5 years At the age of adolescence, development of the breasts and menstruation do not appear. Owing to early epiphysial fusion these patients are short, stocky, and muscular, with coarse hair on the face, abdomen, thighs and legs.

The Juvenile Form (Adrenal Virilism) The juvenile form of the adrenogenital syndrome usually occurs in girls. It rarely occurs in boys When it does occur in boys several children of the same family may be affected

In juvenile virilism the child may have been thought to be a pseudohermaphrodite from birth or the anomaly may have gone unobserved until evidences of virilism appear.

The growth of the long bones usually has proceeded rapidly but subsequently ceases because of premature closure of the epiphyses. Elongation of the spinal column follows The adolescent consequently may be tall with long arms and legs

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In the adult form of the adrenogenital syndrome there is a retrogression of the

normal female sex characteristics. The female sex characters are gradually replaced by the male type of bodily contour and voice, and by hypertrophy of the clitoris and cessation of the menses. The mental perspective is that of a man. There is a striation of the thighs and abdomen similar to that which occurs in the Cushing syndrome.

In the androgenital syndrome, or adrenal virilism, the concentration of the 17-ketosteroids in the urine is definitely increased In the presence of bilateral hyperplasia of the adrenal cortex the concentration of 17-ketosteroids in the urine is from 5 to 30 times the normal In the presence of adrenal adenoma the concentration of the 17-ketosteroids in the urine may reach 100 mg per day. In the presence of adrenal carcinoma the concentration may exceed 200 mg. per day. The beta reaction of the 17-ketosteroids (mainly dehydroisoandrosterone) is markedly increased over its usual 5 to 15 per cent of the total 17-ketosteroids in the presence of adrenal cortical adenoma or carcinoma.

The administration of cortisone to a patient who has adrenal virilism will reduce the concentration of the 17-ketosteroids If the adrenal virilism is due to carcinoma, administration of cortisone is without effect on the urinary steroid content

In boys, as has been stated, precocious puberty may be due to hypothalamic lesions, constitutional precociousness or tumors of the Leydig cells of the testis In these conditions the concentration of the 17-ketosteroids is consistent with the sexual development of the child On occasions the concentration will be increased to 100 mg per day in the presence of Leydig cell tumors In precociousness due to hyperfunctioning of the adrenal cortex the concentration of the 17-ketosteroids is greatly increased.

Tumors of the Adrenal Cortex. The manifestations of adrenal cortical hyperfunction as observed in Cushing's syndrome and the adrenogenital syndrome have been briefly described Moreover, it was emphasized in these descriptions that *hyperfunction of the adrenal cortex was often due to hyperplasia but might be* due to adenomas or adenocarcinomas.

In cortical adrenal tumors the patient may have features of both Cushing's syndrome and the adrenogenital syndrome In the presence of a hyperfunctioning adrenal cortical tumor the symptoms may be dependent on age and sex For instance, in boys there is sexual and somatic precocity In girls there is a type represented by heterologous sexual and somatic precocity and a type represented by homologous precocity characterized by uterine bleeding and enlargement of the breasts. In men hyperfunctioning tumors may produce feminization, while in women there may occur varying degrees of virilism. A hyperfunctioning adrenal cortex may produce symptoms which are independent of age and sex In these patients there is an altered habitus dependent on facial and abdominal obesity, kyphosis and thin arms and legs.

Either oligomenorrhea or amenorrhea is often an early symptom of hyperfunctioning adrenocortical lesions among adults. Generally hot flushes do not occur Impotence of men may be regarded as the homologue of the amenorrhea that occurs among women. Amenorrhea or impotence may occur in conjunction with either adrenocortical tumor or hyperplasia

In most instances of slowly developing adrenocortical tumors the patients are women after the age of puberty and before the menopause These women tend to acquire masculine physical attributes such as hirsutism and enlargement of the clitoris, and tend to become mesomorphic in somatic type.

In rare instances a man may have an adrenocortical tumor *which causes* enlargement of the breasts, impotence and feminine habitus.

Either men or women who are affected by these tumors are usually miserable *because of their* repulsive appearance. However, some show a remarkable capacity to make the necessary psychic adjustments.

The diagnosis of virilism associated with adrenal cortical tumor is made definite only by histologic examination of the tissue obtained by surgical exploration and biopsy. In some instances diagnostic information may be had by the performance of intravenous pyelography which may reveal displacement of the kidney downward with flattening of the upper calyx.

The information obtained from hormonal determinations is as follows Increased excretion of urinary gonadotropin is indicative of the menopause or a tumor composed of chorionic cells and excludes adrenal cortical hyperfunction. Normal concentration of estrogen is of no diagnostic significance. Increased concentration suggests adrenal cortical hyperfunction (tumor)

Steroid Diabetes. Sprague defines steroid diabetes as a diabetic state resulting from an excess of adrenal steroids (cortisone and hydrocortisone). These steroids impair both carbohydrate and protein metabolism and interfere with the action of insulin.

It seems that the presence of some adrenal steroids is necessary for the maintenance of diabetes mellitus for many of the features of the disease disappear if the adrenals of the diabetic are destroyed or removed, and the diabetic state is restored if cortisone or hydrocortisone is administered

Steroid diabetes is limited to patients with spontaneous adrenal cortical hyperfunction of the type with Cushing's syndrome and to some patients who are receiving cortisone, hydrocortisone or corticotropin in large doses In diabetes mellitus there is no convincing evidence of hyperfunction of the adrenal cortex, except transiently, or during severe diabetic acidosis Insufficiency of the islet tissue increases the likelihood that diabetes will result from the presence of excessive amounts of adrenal steroids

Tumors of the Adrenal Medulla (Hyperadrenalism). The adrenal medulla elaborates epinephrine, which stimulates the sympathetic nervous system and, briefly stated, instantly prepares the individual for fight or flight or whatever response the situation demands This preparation is manifested by a dilatation of the pupils, increased cardiac output, contraction of the arterioles, dilatation of the bronchioles and mobilization of blood sugar from the stores of glycogen

The chemically and pharmacologically closely related compound norepinephrine also is present in the medulla as well as throughout the mammalian body

Epinephrine and the corresponding primary amine 1-norepinephrine (noradrenaline, arterenol) normally exist in the mammalian body Norepinephrine was first shown to be present in significant amounts in human beings by pharmacologic and chemical methods 1-norepinephrine is believed to function as excitor sympathin

Epinephrine, within a physiologic and therapeutic range, acts as an over-all vasodilator and causes hypertension only by increase of cardiac output. Norepinephrine functions as an over-all vasoconstrictor without change or only slight decrease of cardiac output It may therefore be conceived as being the sympathetic mediator of over-all vasoconstriction in human beings

The injection of norepinephrine causes within 30 seconds an abrupt rise in the blood pressure which lasts 5 to 8 minutes However, the ventricular rate shows only a slight and transient increase The average increase in the ventricular rate in 10 patients with complete heart block studied by Nathanson and Miller was 5 beats per minute After the administration of epinephrine, there was a pronounced and sustained increase in the ventricular rate, the average increase being 29 3 beats per minute.

It appears, therefore, that epinephrine, in contrast to norepinephrine, possesses both a potent pressor and a cardiac-stimulating action. One of the deductions to be made from these observations is that the presence in the body of a potent sympathomimetic pressor agent with little or no cardiac-stimulating action suggests the possible participation of the sympathetic nervous system in the genesis of essential hypertension

There are four types of tumors which arise in the adrenal medulla: (1) the ganglioneuroma, (2) the sympathogonioma or neurogonioma, (3) the sympathoblastoma and (4) the pheochromocytoma or chromaffinoma

The ganglioneuroma is benign and usually gives no symptoms. The sympathogonioma and sympathoblastoma are highly malignant and occur in infancy or childhood.

Pheochromocytoma (*Chromaffinoma*). The pheochromocytoma or chromaffinoma is the only one of the tumors of the adrenal medulla having hormonal activity. The tumor arises from differentiated chromophil cells which secrete epinephrine or norepinephrine Its symptoms are accounted for by the excessive secretion of combinations of these compounds These tumors may be present in many parts of the body, wherever sympathetic ganglia are situated Pheochromocytomas occur in both adrenals in some cases When the tumors cause hypertension they have been situated in or near the adrenal gland or glands

Paroxysmal attacks of hypertension are characteristic. They may recur at long intervals or as often as several times a day They last minutes to hours, tend to increase in frequency and are often precipitated by emotion, pressure over the tumor, straining, or lying in certain positions These attacks are not present in more than one third of patients who have pheochromocytoma and similar attacks may occur in those who do not have pheochromocytoma

The attack commences with a feeling of weakness and apprehension, palpitation and headache, progressing to a pounding in the chest and throbbing in the head so severe that prostration ensues. These symptoms are commonly associated with pain in the abdomen, chest, back or extremities, nausea, vomiting, drenching sweats and exhaustion

have an excessive rise in blood pressure after immersing a hand in ice water one minute Elevated pressures of 20 mm in systole and 15 mm in diastole are considered abnormal, whereas, a normal or a negative response is common in patients who have pheochromocytoma In the upright position the systolic and diastolic pressure of ordinary hypertensive patients does not commonly fall below the levels in the horizontal position Similarly, the pulse rate does not rise more than 20 or more beats per minute. Most patients with pheochromocytoma have postural tachycardia and, in addition, about half of these have postural hypotension. An intermittent elevation of the body temperature, not necessarily related to paroxysmal symptoms, is found in more than 7 of every 10 of these patients. The determination of the concentration of blood sugar is diagnostically useful A greater concentration than 120 mg per 100 ml is significant Glycosuria may also be found with or without increased blood sugar. An increased basal metabolic rate of +20 per cent is frequent in those who have pheochromocytoma

Roth and Kvale observed that patients with pheochromocytoma responded to the intravenous injection of 0.0125 to 0.025 mg. histamine base with a sudden rise of blood pressure, amounting to as much as 200 mm. systolic and 100 mm. diastolic. The characteristic symptoms of a paroxysmal attack, including circumoral pallor, pilo-erection and sweating, were reproduced

Diagnosis. The diagnosis of pheochromocytoma can be made if there are paroxysmal attacks of hypertension, excessive sweating, peripheral vasomotor phenomena, a normal cold-pressor response, postural tachycardia and hypotension, and elevation of temperature, blood sugar and basal metabolism. *The induction of an attack of paroxysmal hypertension at will by the injection of histamine confirms the diagnosis of pheochromocytoma.*

Adrenal tumors, other than pheochromocytoma, sometimes cause hypertension. Elevated blood pressure is one of the symptoms of Cushing's syndrome, whether due to adrenal tumor or of pituitary origin

The pituitary gland (hypophysis cerebri) is situated within the small cavity of the sphenoid bone (the sella turcica). It is an ovoid reddish gray mass which is readily separated into the anterior and posterior lobes.

The staining reactions of the cells of the pituitary gland are often referred to in discussion of the origin of the pituitary hormones For instance, some of the cells react to the acid dye, eosin, and therefore are spoken of as acidophilic or eosinophilic. Other cells react to the basic dyes, methylene blue or hematoxylin, and are called basophilic Still other cells possess the quality of staining very poorly or not at all and these are designated chromophobic cells

The chromophobes do not produce hormones but are probably precursors of basophils or acidophils. The *growth hormone* is produced by eosinophils; the *follicle-stimulating hormone* is produced by basophils, and *vasopressin* and *oxytocin* are produced by pituicytes The pituicyte is any one of the fusiform cells composing most of the pars nervosa of the pituitary body The origin of the other hormones is indeterminate at the present.

The adrenal medulla and the neurohypophysis are derived from the nervous system, possess a rich nerve supply, and are directly affected by neural impulses It seems likely that much of the nervous control of the endocrine system is mediated through the pituitary The glands which are specifically susceptible to the pituitary hormones are the thyroid, the adrenals, and the gonads These glands are referred to as *target glands*

The concentration in the blood and tissues of the pituitary hormones seems to regulate pituitary function as well as the production of hormones by the thyroid, gonads and adrenal glands. A circulating hormone from some other gland, if of sufficient concentration, may inhibit the secretion of its specific tropin by the pituitary gland and may stimulate the pituitary to secrete a different tropin Such a relationship between the pituitary gland and the ovaries is believed to be responsible for the menstrual cycle

Hypersecretion or deficiency of the thyroid gland, the adrenal glands or the gonads may be due to a disorder in one of these glands, in the pituitary, or in the brain. It is thus evident that the same symptoms may result from a lesion in any of these three different organs

Lesions in the *hypothalamus* may be accompanied by either excessive or diminished activity of the pituitary

The pituitary may be affected by *metabolic disturbances* such as severe malnutrition, vitamin deprivation, or disease Such deprivations may lead to the symptoms of generalized pituitary deficiency with termination of the menses

HORMONES OF THE PITUITARY GLAND Six distinct hormones are elaborated by the *anterior lobe* of the pituitary, namely, thyrotropic, adrenocorticotropic, follicle-stimulating, luteinizing, luteotropic, and the growth hormone. The posterior lobe of the pituitary elaborates one hormone which contains the active principles oxytocin and pitressin.

The *thyrotropic hormone* (TSH or TTH) by stimulating the thyroid causes hypertrophy and hyperplasia of this gland and thus increases its ability to take up and fix iodine. The concentration of total and protein-bound iodine in the serum also is increased The effects are similar to those produced by thyroid substance

The *adrenocorticotropic hormone* (ACTH) determines the carbohydrate-regulating function of the adrenals Another tropic hormone in addition to ACTH may influence the secretion of the adrenal androgen

The *follicle-stimulating hormone* (FSH) is necessary for the growth of graafian follicles after they have reached the stage of formation of antra. This hormone, acting with the *luteinizing hormone* (LH), influences secretion of estrogen, maturation of the follicle, ovulation, and formation of luteal tissue. In the male, FSH with LH stimulates the development of the seminiferous tubules and the production of spermatozoa

The *luteinizing hormone* (LH) induces ovulation and the formation of a nonfunctioning corpus luteum It controls the secretion of testicular androgen

The *luteotropic hormone* (LTH), *lactogenic hormone* or *prolactin* maintains the corpus luteum for about 2 weeks and causes the release of progesterone from it It

initiates lactation in mammary glands which *have undergone alveolar development* during pregnancy.

The follicle-stimulating, luteinizing and luteotropic hormones are all called gonadotropic hormones. Estrogen, which is responsible for most of the development of the female sex organs, is dependent primarily on follicle-stimulating hormone, whereas male sexual development *is brought about by androgen under the influence of luteinizing* hormone.

The *growth hormone* or *somatotropic hormone* (SST or STH) acts directly on the growth of body tissues without the mediation of other glands. It exerts a specific influence on the proliferation of cartilage and bone, probably through its ability to increase *protein anabolism* The growth hormone exerts important effects on carbohydrate metabolism

The *posterior lobe* of the pituitary gland elaborates one hormone which contains two principles, oxytocin (pitocin) and vasopressin (pitressin). Oxytocin acts mainly on the muscle of the uterus Vasopressin has little or no action on the uterus but acts more vigorously on the musculature of the intestines It exerts a profound influence on salt and water metabolism

Diseases of the Pituitary Gland. Symptoms of pituitary disease may arise from primary disease of the pituitary gland itself or from disease of the adjacent brain tissue When the gland itself is affected, the symptoms are primarily endocrine in nature, while those of the adjacent brain tissue may be manifested as either endocrine disturbances or those of intracranial hypertension In some instances there is a combination of intracranial hypertension and endocrine disturbance In a discussion of diseases of the pituitary gland there can be no categorical separation *of the diseases which give mainly endocrine disturbances from those which give* symptoms predominantly of intracranial hypertension

There are a number of diseases of the pituitary, usually tumors, which produce symptoms from pressure on the brain tissue and nerve tracts about the pituitary. These disorders are enumerated as (1) adenomas of the anterior lobe, (2) congenital tumors arising from the hypophysial duct and (3) other intracranial growths in the region of the sella turcica such as aneurysms of the circle of Willis, gliomas and gummas *Secondary growths, often metastatic from carcinoma of the breast or* pancreas are occasionally present in the posterior lobe, by their pressure effects, these as well as other pituitary tumors may destroy the pars nervosa and give rise to diabetes insipidus

Symptoms attributable to pressure on the hypothalamus are obesity and failure of the reproductive organs Interruption of the hypothalamicohypophysial tract results in polyuria and diabetes insipidus by interfering with the function of the pars neuralis *Involvement of the corpora mammillaria and the adjacent structures* produces somnolence

Endocrine Diseases of the Pituitary Gland. Endocrine diseases of the pituitary are classified as (1) those due to a deficiency of the hormone of the anterior lobe such as Simmonds' disease and infantilism, (2) those due to excessive activity of the hormone such as acromegaly and gigantism, (3) those due to *deficiency of* the posterior lobe and (4) those due to associated disorders of the pituitary and hypothalamus

Hypopituitarism (*Anterior Lobe*) The essential lesion of hypopituitarism is the destruction of the anterior lobe of the pituitary gland Conditions capable of causing necrosis of the pituitary consist of tumors, cysts, gumma, massive tuberculous necrosis, granulomas of unknown etiology, hypophysectomy and healed postpartum necrosis of the anterior lobe of the pituitary However, *a common cause of* hypopituitarism is massive focal atrophy, which occurs only in women and is nearly always of postpartum *origin. The necrosis is present in* patients who have severe hemorrhage and circulatory collapse These patients die at any time within a few hours postpartum onward.

Hypophysial Cachexia (*Simmonds' Disease*) The occurrence of loss of weight, amenorrhea and a low basal metabolic rate in a woman whose symptoms date from postpartum hemorrhage and collapse warrants, in the opinion of Escamilla and Lisser, a clinical diagnosis of Simmonds' disease These workers emphasized a confusion of Simmonds' disease with anorexia nervosa Anorexia nervosa may occur in either sex at any age but it occurs more frequently in young girls who have not been pregnant than in other persons

Severe deficiency of the pituitary function is manifested clinically, according to Sheehan, by a syndrome made up of the following characteristics. in many cases a history of severe circulatory collapse as a result of hemorrhage and shock at a delivery; atrophy of the gonads and genital tract with complete amenorrhea; impotence and loss of libido; complete loss of pubic and axillary hair, absence of normal skin pigment; a typical flabby facies with thinning of the eyebrows and pallor, increased sensitivity to cold, weakness, mental torpidity with slow speech; a low basal metabolic rate; very low urinary excretion of 17-ketosteroids, insulin sensitivity and hypoglycemia unresponsiveness, and a tendency to spontaneous hypoglycemia and coma Sheehan has stressed that patients with hypopituitarism face the grave danger of a particular type of coma which is often fatal

On *examination* the patient is apathetic and exhausted, assumes all the appearance of extreme senility, and may appear to be suffering from myxedema or Addison's disease. The administration of desiccated thyroid often induces hypoglycemia or an addisonian crisis There is marked sensitivity to insulin, a fraction of the usual dose will induce a reaction. This sensitivity is utilized as a test for the differentiation of hypopituitarism and Simmonds' disease from myxedema and other cachectic conditions which resemble it clinically The response of this hypoglycemia to epinephrine is slight.

In moderate degrees of pituitary insufficiency the excretion of 17-ketosteroids is reduced to less than 2 mg per day In extreme hypopituitarism, as in Simmonds' disease, the excretion is less than 0 5 mg per day In anorexia nervosa the excretion usually varies from 2 to 15 mg. per day In myxedema also it may be as low as 1 to 2 mg.

The *diagnosis* of hypopituitary cachexia (Simmonds' disease) depends on the presence of a low basal metabolic rate and on failure of the blood sugar to return to within 10 per cent of its fasting level in 2 hours after the intravenous injection of insulin. There is a low urinary excretion of 17-ketosteroids, and a positive result of the water test for adrenal insufficiency

In differential diagnosis it will be remembered that abnormal insulin tolerance curves are also present in hyperinsulinism, Addison's disease, anorexia nervosa, severe hepatic disease and malnutrition

The treatment of anterior pituitary necrosis has thus far been disappointing since the administration of the hormonal secretions of anterior pituitary extracts has not been efficacious

Hyperpituitarism (*Gigantism and Acromegaly*) Gigantism and acromegaly are associated with eosinophil cell or mixed cell adenoma which may extend out of the sella turcica and involve the base of the brain, or may encroach upon or penetrate the sphenoidal sinuses In some the pituitary remains normal in size, but in such cases there is an increase in the number of eosinophilic cells Hyperactivity of the anterior lobe of the pituitary gland causes gigantism in the adolescent and acromegaly in the adult In about one half of these patients the disease first appears in the third decade of life, but it does not develop fully before 45 to 50 years of age. Acromegaly may be present for thirty to fifty years and never pass into a hypopituitary stage, and it is therefore compatible with normal physical and intellectual vigor.

The *symptoms* develop slowly in *gigantism*. The growth during childhood is not

noticeable, for it is uniform and symmetric. The first parental suspicion that there is something wrong with the rapidly growing child is aroused when they realize that it has reached giant proportions for the age On examination the signs of the pituitary disturbance manifested by weakness, a dry skin, subnormal temperature, low basal metabolic rate, low blood pressure, a high sugar tolerance, and a low resistance to infection are revealed. The presence of a superimposed acromegalic gait and the other unequal growth characteristics of acromegaly may be evident.

The average age at death of giants is 21 years, though an occasional one may live to 40 or 50 years

There are six diagnostic features of gigantism. (1) *The patient usually is less* than 20 years of age (2) There is an overgrowth of cancellous bones and delayed union of the epiphyses (3) The hands and feet are very large. (4) The jaws are elongated and the cheek bones and supra-orbital ridges are prominent (5) Gonadal atrophy is present (6) The sella turcica is enlarged and may be eroded.

In diagnosis it is remembered that the patient who has pituitary gigantism differs from the genetically large individual in length of the extremities and size of the viscera Moreover, the pituitary giant is less likely to have the genealogic history of tall men and women in the family

The first *symptoms of acromegaly* are often increased appetite, fatigue, muscle pains, headache, apathy, disturbances of vision, somnolence, polyuria and voice changes occurring in an adult The symptoms of acromegaly commence so insidiously that the patient is unaware of his voracious appetite His complaints of fatigue may cause his family to remind him of the excessive amounts of food consumed. Soon the patient and his family are aware of the changes in his facial features The supra-orbital ridges are enlarged, the lower jaw elongates and becomes wider and extends forward, the head, the hands, the feet enlarge, the gait is an awkward one and the muscles tire easily

The symptoms of intracranial hypertension may supervene at any time during the course of the illness Those due to the pressure of the intracranial tumor (headache, visual defects, fits and vomiting) are *common* *Often, however,* there are no symptoms except increase [illegible]
of the hat, gloves or shoes [illegible]
of acromegaly may appear during pregnancy. This has been referred to as a [illegible]tive type

On *examination* of the acromegalic there may be no noticeable increase in size. There is only disproportionate increase in the size of the head, particularly the lower *jaw, and the hands An occasional patient may be of excessive size* which was obtained prior to the disproportion in the size of the parts

There is thickening of the epidermis with hypertrophy of the papillae of the skin As the result of thickening of the subcutaneous tissues there are furrowing of the skin and coarsening of the features As the disease progresses, there are impotence and sterility due to atrophy of the testes or ovaries.

The growth of the mandible separates the teeth of the lower jaw and gives prognathism. The *chin is curved and turns upward The nose,* lips, and tongue are broadened and enlarged The malar bones and the supra-orbital ridges are prominent. The hands and feet enlarge and broaden, and the ends of the phalanges thicken and become broad (spade-shaped) There is an enlargement of the viscera The larynx may become enormously enlarged

The roentgenologic examination in acromegaly reveals the enlargement of the sella turcica, the jaw, head, and extremities There is an increase in the anterior dimensions of the bodies of the vertebrae, *particularly as seen in lateral films* of the thoracolumbar portion of the spinal column.

Exostoses due to periosteal overgrowth are frequent The *flat bones,* particularly the calvarium, may be greatly thickened, and the frontal sinuses become enlarged.

The concentration of phosphate in the blood is increased (4 to 6 mg per 100 ml), but other biochemical laboratory studies are of little aid in the diagnosis of the condition.

The hypersecretory activity of the hypophysis induces certain metabolic changes. Exophthalmos is common with an elevation of the basal metabolic rate. The thyroid is enlarged and may undergo colloid degeneration Glycosuria is frequent. True diabetes occurs in about one eighth of all cases This diabetes differs, however, from ordinary diabetes mellitus, for it may spontaneously undergo a permanent or temporary amelioration of all the symptoms of diabetes

There are six diagnostic features of acromegaly. (1) The patient is more than 20 years of age. (2) There is enlargement of the acral parts of the body (bones and soft parts of the hands, feet and face) (3) There is enlargement of the sella turcica by roentgenologic examination (4) There is thickening of the epidermis with infiltration of the subcutaneous tissues resulting in wrinkling of the skin of the face and scalp (5) There are associated endocrine disturbances, for instance, increased metabolic rate and perhaps diabetes mellitus but rarely diabetes insipidus. (6) Intracranial hypertension, exophthalmos, increase in anterior dimensions of the vertebrae of the thoracolumbar spine—one or all may be present

In the diagnosis of either gigantism or acromegaly there may be no evidence of pituitary adenoma or hyperpituitarism at the time of the examination Both of these conditions can occur presumably from an increase in the eosinophilic cells attended by a decrease or an absence of the basophilic cells of the anterior pituitary part of the gland. The hyperpituitarism may have run its course and been supplanted by the symptoms of pituitary insufficiency

Hypogenitalism and Puberty in Boys. The testes are thought to be dependent on two pituitary gonadotropic hormones The first, the follicle-stimulating hormone, acts on the tubules; the second, the luteinizing hormone, affects the Leydig or interstitial cells Spermatogenesis, therefore, cannot take place without function of the Leydig cells, so that the two hormones must be present to produce normal sexual function and development

The term hypogenitalism means a disproportionate smallness of the external genitalia in relation to somatic development Up to the age of 11 or 12 years the testes and the penis undergo little change in size The testicle is approximately 1 7 cm long and 0 8 cm wide. With puberty, which usually begins at 11 or 12 years of age but may be delayed to 14 or 15 years of age, even though growth is normal, the testes may not increase in size

In the fat boy, even with beginning pubescence, the genitalia often appear small because they are partially submerged in adipose tissue The size of the testicle may be estimated by volume and by linear measurements The volume of the testicle is determined by drawing the scrotal skin tightly over the testicle and comparing its volume with that of known standards Any testicle which is approximately 2 ml in volume before pubescence may be considered normal, but those of less than 2 ml volume are regarded as instances of hypogenitalism

The *body types* which may result from *delay or failure of pubescence* are. (1) slight eunuchoid skeletal proportions, but these are outgrown and eventually maturity is normal, (2) eunuchoid with hypogenitalism and eunuchoid skeletal proportions, namely, long arms and legs, when eunuchoidism is due to primary testicular failure there are occasionally more body hair and sexual hair and fewer skeletal changes, (3) gynecomastia and varying degrees of eunuchoidal changes Aspermia is present owing to tubular hyalinization, at least late in the disorder. The breasts show well marked and pigmented areolae

Boys of 14 years of age may show a wide range of skeletal maturation, which as a rule accompanies genital development If obese boys of 14 with retarded pubes-

cence are of average or greater height, only delayed pubescence and eunuchoidis need to be considered

Enlargement of the breasts in the fat boy may be due to adipose tissue only a is unimport [illegible] aid, but in the nonobese child this is a fairly reliab sign of pube [illegible] subsides spontaneously in the norm pubescent, [illegible] gynecomast with aspermia is suspected (see [illegible]

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Diseases of the Posterior Lobe of the Pituitary (Neural Division). Th posterior lobe of the pituitary elaborates (1) the antidiuretic hormone, which con trols the secretion of urine by the kidneys and regulates the water and electrolyt balance of the body fluids, (2) the oxytocic hormone, which stimulates the uteru during parturition, (3) the combined extract of the posterior pituitary, which act on smooth muscles in many parts of the body including those of the arteries Th effect is one of smooth muscle contraction

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Hypofunction of the Posterior Lobe of the Pituitary Gland (*Diabete Insipidus*). Diabetes insipidus may appear at any time during infancy or adult life In some families more than one member is affected Traumatic lesions, especially ones associated with fracture of the base of the skull, and infections such as men ingitis or encephalitis may cause the syndrome Once the entity has appeared, i persists However, remissions may be observed A normal life span may then be enjoyed

The *symptoms* of the disease are due to a deficiency of antidiuretic hormone. There is intense thirst, polyuria, and dryness of the mouth and skin

The quantity of urine excreted per day depends on the extent of satisfaction of the thirst Excretion of 8 to 12 liters is common The loss of a large quantity of urine results in an excessive loss of heat The heat loss accounts for the hypothermia and the hyperorexia The fatigue and loss of strength and ambition are related to the nervous tension Obstinate constipation is consequent to the dehydration Head- ache, dizziness, and pain in the back and legs may occur Often the patient is tired, apathetic and irritable

On *examination* there may be found intracranial disturbances such as visual field defects, papilledema, ocular palsies, nausea, vomiting and dizziness Usually the blood pressure is normal

The urine is pale and free of sugar, sediment and albumin The specific gravity is 1.001 or 1.002, never more than 1 005 The excretion of chloride is reduced The phenolsulfonphthalein excretion, glomerular filtration rate, urea clearance, creatinine clearance, and results of intravenous urography tend to be normal

The concentration of blood cells and of chemical constituents of the blood varies in different patients. The sodium chloride and hematocrit may be decreased

After the injection of 1 ml of pituitrin the urine volume and specific gravity usually become normal in the patient who has diabetes insipidus

In *diagnosis* the specific gravity of the urine in diabetes insipidus is *less than* 1.005. If the specific gravity exceeds 1 005, the condition is probably a polyuria

associated with psychic disturbances or nephritis Patients who have polyuria associated with nephritis rarely excrete more than 5 liters in 24 hours. There usually is a history suggesting nephritis, hypertension, retinitis, sedimentary changes in urine, decreased urea clearance, and decreased phenolsulfonphthalein excretion.

The polyuria due to a lack of psychic control varies more in degree than does that of diabetes insipidus or nephritis. When water is withheld for 12 hours, the patient who has diabetes insipidus complains of intense thirst, nervousness, apprehension, weakness and hypothermia. Moreover, there is a continued excretion of large quantities of hyposthenuric urine. The person who has psychogenic polydipsia and polyuria can tolerate the water deprivation without any great discomfort

Tumors of the Pituitary Gland. ***Adenomas.*** The adenomas of the pituitary gland arise from the anterior lobe They are composed of cells giving both chromophil and chromophobe reactions

Chromophobe adenomas are the commonest of the lesions in the region of the optic chiasm Lesions in this region occur in the following order of frequency adenoma of the pituitary, *suprasellar cysts* and *craniopharyngioma, glioma* of the chiasm, meningioma arising from the floor of the third ventricle, rare tumors (chordoma, cholesteatoma), chronic arachnoiditis and aneurysmal dilatation of the carotid artery.

Chromophobe adenomas occur from the third to the fifth decades of life, and cause great enlargements of the sella They do not give rise to symptoms which might be attributed to hypersecretion of some humoral principle

These adenomas are benign growths, but malignant tumors occasionally are encountered. The malignant growths do not metastasize but may give rise to a rapid progression of symptoms with extension of the tumor into the adjacent skull, brain and nasopharynx.

The *symptoms* of the chromophobe adenomas result from the pressure which these growths exert on the adjacent regions of the hypothalamus, the optic chiasm, or on the rest of the gland Impairment of vision is an early symptom, with atrophy of the optic nerve head as observed by the ophthalmoscope, perimetric bitemporal field defects, and inability to read when the macular bundle is affected Obesity, amenorrhea and impotence are frequently early symptoms, which are probably hypothalamic in origin The atrophic changes in the skin and hair and the evidences of general cachexia observed as the tumor enlarges are attributable to hypophysial deficiency due to destruction of the chromophilic cells Symptoms of intracranial hypertension may be present

On *examination* there often are found evidences of intracranial hypertension There is bitemporal hemianopsia The visual field defects in chromophobe tumors tend to be regular and symmetric in outline

The roentgenogram reveals the enlarged sella The final diagnosis is established by histologic study of the adenoma, which has been localized by means of the ventriculogram and removed surgically

Craniopharyngiomas comprise a variety of growths which appear in the middle line above the sella adjacent to the infundibulum and optic chiasm They are of congenital origin and arise from cellular rests of the embryonic hypophysial duct. They may be designated as cysts of Rathke's pouch, interpeduncular or suprasellar cysts Rare tumors, giving rise to manifestations similar to those produced by craniopharyngiomas, are cholesteatomas, dermoid cysts, chordomas, and teratomas

Associated Disorders of the Pituitary Gland and the Hypothalamus. The association between the pituitary gland and the other endocrine organs is dependent on the direct anatomic and physiologic connections between them These connections are presided over by the autonomic nervous system The hypothalamus participates in both metabolic and reproductive functions which are also involved in endocrine disorders The close proximity of the pituitary and the hypothalamus predisposes to lesions of either tissue affecting the function of the other.

The hypothalamus is the central neuroglandular mechanism which controls the basic rhythms of organic life The fundamental patterns of personality are situated

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Enlargement of the breasts in the fat boy may be due to adipose tissue only and is unimportant as a diagnostic aid, but in the nonobese child this is a fairly reliable [illegible]

[illegible] Diseases of the Breast, Chapter [illegible]).

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gens or estrogens with an increased excretion of gonadotropic substance, whereas in primary pituitary deficiencies there may be a diminished excretion of both

There may be an increased carbohydrate tolerance due to decrease in the secretion of an insulin-antagonizing hormone. The basal metabolic rate is variable. There may be retention of fluid or the other extreme, diabetes insipidus may be present. Often the concentrations of plasma chlorides and uric acid are increased.

Roentgenograms of the skull rarely reveal abnormal changes Occasionally enlargement and erosion of the sella indicative of an expanding lesion, calcification within the sella, or a sella considerably smaller than normal may be present.

The *diagnosis* of adiposogenital dystrophy is established by combination of symptoms and findings as described. Many patients do not present the characteristic findings.

The Hypothalamus and Hypergonadism (*Precocious Puberty*) Precocious sexual development may result from tumors or disease of the hypothalamus.

Precocious puberty secondary to hypothalamic disorders may follow encephalitis, in association with cysts of the third ventricle At any age precocity may be the presenting symptom in cases of tumors of the hypothalamus without recognizable evidence of intracranial disease. This precocity may be accompanied by somnolence, adiposity, diabetes insipidus and polyphagia

In hypothalamic precocity there is maturity of both gonads and secondary sex characters. This development may be a result of hypothalamic disease, or may occur in association with the pineal tumors and paraphyseal cysts, or without any demonstrable lesion.

Precocity secondary to adrenal and gonadal disturbances is characterized by normally developed external genitalia and secondary sex characters but without gonadal maturity.

Syndrome of Sexual Precocity, Areas of Skin Pigmentation and Fibrous Dysplasia of Bone. This syndrome occurs in girls There are sexual precocity and unilateral brown macular skin lesions associated with disseminated areas of osseous rarefaction The skin lesions are present at birth or soon thereafter. The bone lesions are not manifested until pathologic fractures occur Deformities of bones may be incident to rarefaction or to overgrowths Overgrowths of bone may impinge on the optic nerves, causing visual field disturbances, if situated in the orbit they may cause unilateral proptosis. Overgrowth of the facial bones may obliterate the nasal sinuses and cause facial asymmetry Sclerotic overgrowth of bone at the base of the skull may occur.

The areas of rarefaction occur most commonly in the long bones Calcium and phosphorus metabolism are normal

Nonendocrine Disorders of the Hypothalamus. ***The Hypothalamic Syndrome.*** This syndrome, a nonendocrine disorder, is characterized by the presence of proptosis, paresis of the muscles of the eyelids, edema of the conjunctivae, and retrobulbar pain.

The hypothalamic syndrome may be combined with affective psychic and vegetative disturbances involving sleep, body temperature, and vasomotor and secretory functions. Abnormalities in fat metabolism and sexual function, narcolepsy, diencephalic epilepsy, catalepsy, affective loss of tone, and the Wilson and the Korsakow syndromes are associated with lesions in the hypothalamus, and also interference with other parts of the brain connected to the hypothalamus is concerned in these disorders.

Body Temperature. The hypothalamus is the center for *temperature control* of the body. There are other secondary centers for temperature control. This exact location is disputed Anteriorly situated lesions are likely to impair the regulation against heat, while the regulation against cold remains intact; posteriorly placed lesions involve a disturbance in regulation of both heat and cold. Lesions, too, of the

in the hypothalamus, though they are presided over by the frontal lobe Lesions of distant parts of the brain with which the hypothalamus is connected or endocrine disease may produce the symptoms attributed to the hypothalamus. Likewise disease of the hypothalamus may produce syndromes similar to those caused by endocrine glands or diseases of distant parts of the brain.

Through its connections the hypothalamus and its supra-optic nucleus form a functional unit. Lesions in any part of this tract result in *diabetes insipidus Gonadal functions* are mediated through the hypothalamus Lesions of the floor of the third ventricle may cause hyperglycemia and glycosuria, and similar effects may be induced by excitation of the hypothalamus and its tuberal component

Diseases of the hypothalamus may have as manifestations obesity, sexual precocity, or genital dystrophy in which the initial symptoms were referred to abnormalities in other vegetative functions, or in affective psychic disorders Lesions of the hypothalamus are prone to originate disturbances in psychiatric and vegetative functions which seem to be of an endocrine origin

The hypothalamic disorders may arise from tumors of the third ventricle and from infections, particularly encephalitis lethargica, syphilitic meningo-encephalitis and intoxications Trauma rarely causes prolonged hypothalamic manifestations.

Dystrophia Adiposogenitalis (*Frohlich's Syndrome*). The pituitary and the region of the hypothalamus are concerned with growth, sexual development, certain phases of metabolism, and obesity.

The cause of dystrophia adiposogenitalis may be intracranial hemorrhage, encephalitis, or possibly toxic suppression or degeneration of the pituitary or adjacent structures following infectious diseases of childhood There are many instances in which no pathologic lesion is demonstrable clinically or at necropsy.

Adiposogenital dystrophy occurs more often in females than in males, but the latter are seen by physicians more frequently because genital infantilism is more conspicuous. The onset may occur at any age Rarely there is a history of excessive weight at birth Often there is a rather sudden and progressive increase in weight, beginning between the ages of 7 and 10 years, which is out of proportion to the food intake

The *symptoms in children* include obesity and genital hypoplasia with regression in the size of the genitalia Patients in whom the disease has been present for some time may become cachectic, owing to the development of Simmonds' disease resulting from destruction of the pituitary gland.

The chief symptoms observed in Frohlich's syndrome in *adult patients* are obesity, faulty skeletal development and genital hypoplasia Polydipsia, polyuria and polyphagia are common, with diabetes insipidus in some cases

The intelligence is normal except for the introspection and self-consciousness which are due to the physical appearance

When the disorder is due to a neoplasm or craniopharyngioma, symptoms arising from increased intracranial pressure, bitemporal hemianopsia, optic atrophy, headaches and somnolence are present

On *examination* the obesity is of the female type with deposition of fat over the mons veneris, mammae, hips, upper part of the thighs, and lower part of the abdomen The reproductive organs have failed to develop. The skin is soft; the hair often is scanty. The hands are plump with tapering fingers The patient is often short, owing to the epiphyses remaining open In men the voice remains effeminate and gynecomastia is prominent.

The genitalia of the male patient should be examined for the presence of undescended testes. If possible the testes should be manipulated in the scrotum and their size estimated. In men the prostate and seminal vesicles, and in the female the pelvic organs, are infantile Hormone assay of the urine may suggest an endocrine disturbance. In primary hypogonadism there may be diminished excretion of either andro-

A *sex reversal in a female child* may have begun in fetal life and the child is a pseudohermaphrodite, or the child may have a persistent urogenital sinus, shallow vagina and hypertrophied labia majora There is too rapid growth in size, muscular development, hirsutism and thus the girl attains the appearances of a male. A sex reversal in postnatal life in a female who is normally developed may be caused by adrenal cortical hyperplasia, or tumor, or it may have resulted from an arrhenoblastoma of the ovary.

When a *sex reversal* occurs in a *normal male* it may result from a feminizing adrenal cortical tumor or perhaps from a chorio-epithelioma There is gynecomastia and perhaps testicular atrophy If the boy is affected when born there is male pseudohermaphroditism The cause in the latter cases is uncertain

The sex traits which are genetically determined and are not directly under the influence of hormones give rise to *sexual dimorphism,* the condition of having some of the properties of both sexes, as in the early embryo and in some hermaphrodites. Persons who have sexual dimorphism or intersexes show no development of secondary sexual characteristics until the usual age of puberty. Prior to puberty a prediction of whether the secondary sexual characteristics will be masculine or feminine cannot be made from the type of gonad present The relative importance of heredity, intrauterine hormones and other endocrine influences cannot be determined Sexual dimorphism includes the early descriptions of the hermaphrodites There are many different types—heterosexual differentiation

The distribution and the degree of growth of hair, aside from that of the scalp, is sexually distinctive. However, an occasional girl or woman who gives no evidence of any endocrine disorder may have a beard or may have a profuse growth of the hair on the body. Growth of hair on the face and the body of women, except in cases in which this is due to a masculinizing tumor of the ovary or adrenal, is likewise hereditary, and endocrine therapy is ineffective treatment In rare instances such a growth of hair will occur as the result of an excessive secretion of androgens

The Sex Hormones. There seems to be an interdependence of the action of the sex hormones with the hormones of the other endocrine glands, for all of the hormones are necessary for the normal growth, development and function of the reproductive system In the absence of the thyroid hormone or the adrenal hormone, for instance, reproductive activities are affected or annulled Deprivation of the essential vitamins or dietary deficiencies cause changes in the gonads Certain hormones that are produced by the gonads, by the hypophysis and by the chorionic tissue exert important action on the reproductive system A variety of these substances is known and they may be assigned, according to their origin, into (1) the pituitary hormones or gonadotropins, (2) the pituitary-like gonadotropic substances and (3) the sex hormones

The *pituitary sex hormones* are derived from the pituitary gland They have been discussed in the section on the description of this gland

The *pituitary-like gonadotropic substances* are formed by the chorionic tissues of the placenta They are found in the placenta, the urine or the blood serum during pregnancy.

The *sex hormones* are the products of the gonads They comprise (1) the androgens, or male hormones, (2) the estrogens, or female hormones and (3) the progestational hormone derived from the corpus luteum

The Androgens or Male Sex Hormones. An androgen is a hormone which possesses masculinizing activities The testicular tissue and urine of men contain the androgens, the male sex hormones It is the present consensus that testosterone represents the male sex hormones However, large doses of testosterone are required in substitution therapy in contrast with the small doses of other hormones Large doses of testosterone will induce normal growth of the prostate and the seminal vesicles in the castrate but fail to prevent hypertrophy of the hypophysis These observations may well indicate that testosterone is only a part or a derivative of the genuine male sex hormone Androsterone, too, probably represents a derivative of the hormone, but retains some of its androgenic activity

gray matter surrounding the third ventricle behind the optic chiasm may induce hyperthermia

Disturbances in temperature regulation and somnia may be observed in craniopharyngiomas, cysts of the third ventricle, and other lesions affecting the hypothalamus.

The hyperpyrexia of hypothalamic origin is not accompanied by the general symptoms resulting from fevers of infectious origin Despite this fact, a *neurogenic hyperpyrexia* accompanied by an increase in the erythrocyte count and an alteration of the differential leukocyte count from the normal may make the neurogenic fever difficult to differentiate from one of an infectious origin However, the neurogenic fever may subside after the administration of phenobarbital. The *infectious fever* may subside after the administration of aspirin (acetylsalicylic acid)

Hypersomnia. Like the hypothalamic syndrome, hypersomnia is nonendocrine in origin There is an inversion of the sleep rhythm, and occasionally narcolepsy, with or without cataplexy, are observed in hypothalamic disorders incident to a viral encephalitis Hypersomnia is frequently present in those who have craniopharyngioma or gliomas involving the floor of the third ventricle Profound sleep may follow surgical operations or an injury in this region

Ulcerations of the lower part of the esophagus, the stomach and the duodenum occur in some who have hypothalamic lesions Disturbances in hepatic function, for instance hyperglycemia and cirrhosis of the liver (Wilson's disease), may be associated with hypothalamic disease

THE GONADS

The gonads, the organs of sex, comprise the testes and ovaries These organs furnish the exocrine elements, the sperm and the ovum, and elaborate hormones for the maintenance of the accessory organs of sex as well as the secondary sex characters.

There are certain terms referring to sex which require mention Ambisexual refers to a trait pertaining to both sexes A secondary sex character occurs normally in but one sex but can develop in either sex A secondary sex character is contrasted with a sex-limited character, a trait which is limited to one sex only The term sex-linked refers to the genes which transmit traits contained in the sex chromosomes An acquired character is a modification produced as a result of the person's (or animal's) own activities or environment. A compound character is one which is dependent on two or more genes for its production A dominant character can develop through the agency of a single gene. It thus appears in the first filial generation and in three fourths of the members of the second filial generation A recessive character is one which requires two allelomorphic genes for full development Thus it often fails to appear (is recessive) in the first filial generation, but reappears in part in the second filial generation

Sexual precocity is sexual maturity at an age younger than expected for the family and the race It is due to disorders arising in either (1) the hypothalamic region of the brain, (2) the pituitary or (3) the gonads In those in whom the disorder is due to a lesion of the brain or the pituitary there is a normal pituitary-adrenal-gonadal relationship and the gonads show normal gametogenic function, whereas in those in whom the disorder is due to an excessive and early production of a sex hormone by a neoplasm or tumor or hyperplasia of the adrenal gland the gonads do not show normal gametogenic function.

Sexual infantilism is the persistence of the infant type of genitalia into adulthood without development of secondary sex characteristics A wide variation exists in the age at which some boys and girls reach maturity—adolescence The normal age for pubescence is controlled by genetic influences (heredity). Permanent sexual infantilism is due to a disorder of (1) hypothalamus, (2) pituitary gland or (3) the gonads

The *congenital absence* of both testes is rare Absence of one testis, with compensatory hypertrophy of the other, and the presence of more than two testes also are rare, while a failure of a testis to descend into its normal position in the scrotum or its displacement in an abnormal position is a common occurrence

Cryptorchism results ultimately in the degeneration of the seminiferous tissue, only the Sertoli and Leydig cells remaining intact A cryptorchid testis is unproductive of spermatozoa, but it usually elaborates the male hormone so that the secondary sex characters remain normal. When cryptorchism is accompanied with evidence of eunuchoidism, there is hypoplasia of the interstitial tissue Destruction of the seminiferous tubules in cryptorchism is apparently due to the elevated temperature of the testicle This can be produced by applying heat to the scrotum

A failure of normal maturation of the gonads at puberty gives rise to a eunuchoid individual with failure of development of the secondary sex characters The voice is feminine, the breasts enlarge, the hair of the head has a feminine contour, and there is neither beard nor body hair The condition is thus comparable with that induced by prepubertal castration If the defect in development involves only the seminiferous tubules, development of the secondary sex characters is normal

In human beings *castration* performed after adolescence does not result in detectable abnormality of body growth Castration of the adult does not always lead to impotence, and the sexual instinct may persist. Eunuchs may copulate up to 25 to 30 years after castration Among castrates because of injuries sexual vigor remains undiminished in some, but in most instances it is decreased from normal, and in many there is almost complete suppression of libido and potentia Castration before puberty initiates an excessively long growth of the bones with a lack of proportion between the length of the trunk and extremities. The epiphysial synarthroses persist beyond the normal age The pelvis resembles the female type, the skull is acromegalic The larynx remains small, the thyroid and cricoid cartilages never ossify, and there is an absence of the pomum adami. The pubic hair is of the female type, the hair on the face and body is scanty. The mammary glands are enlarged and of a virginal female type except that there are small nipples

Hypogonadism may be *acquired* Chronic inanition or avitaminotic deficiencies may induce testicular deficiency Mumps and smallpox may affect the testes, to be followed by extensive fibrosis and atrophy Gonorrhea involves the testes usually by an ascending infection of the urogenital canal, syphilis gives rise to a fibrous orchitis or gummas of the testes, tuberculosis affects the testes, usually secondarily to infection of the epididymis All of these conditions may result in destruction of both the seminiferous tubules and the interstitial tissue and thus lead to hypogonadism. Alcohol and lead may be cited as examples of toxins which may involve the testes Chronic or debilitating disease or malnutrition in childhood may interfere with the normal development of the testes and thus give rise to hypogonadism in the adult Hypogonadism may also arise secondarily to failure of the thyroid, pituitary, hypothalamus or adrenal glands.

Among normal persons the male excretes androgens and estrogens in the urine in a ratio of approximately 2.1, while in the female the ratio is approximately 1:7. In male hypogonadism if testosterone has not been administered there is a reduced excretion of androgenic substances in the urine

The *male climacteric,* presumed to be analogous to the condition commonly observed in women at the menopause, is observed infrequently. Subjective nervousness is the principal manifestation of the disorder Other prominent symptoms in the order of their frequency are loss of potentia, depression, defective memory, fatigability, lassitude, loss of confidence, disturbances in sleep, irritability, fear of impending danger, numbness and tingling of the skin, vertigo, hot flushes, headache, tachycardia, palpitation, fits of crying, and urinary symptoms (Werner).

In some instances, however, an organic basis for justifying the claim that the male climacteric or hypogonadism gives rise to a true clinical entity may be demon-

The male sex hormone seems to be elaborated by the germinal tissue of the testes The testes also contain large amounts of estrogen, the significance of which is unknown

Urinary Excretion of Male Hormone (Androgens). The urine of both the male and the female is androgenic, as manifested by the presence of 17-ketosteroid bodies The normal urinary androgen excretion in men varies from 63 to 68 international units; in women from 42 to 56 units. In male castrates exceedingly small amounts of sex hormone (1 to 3.5 units) are excreted In adrenal virilism there is an exceedingly variable excretion, high (500 units) in some cases, but in others, low or normal. In prostatism the excretion of androgens is decreased below normal. The average daily urinary excretion of estrogen corresponds to from 9 to 12 micrograms of estrone in men and from 18 to 36 micrograms in women. The significance of estrogens in the male organism is unknown

Small amounts of androgens are excreted in the urine prior to puberty, and the greater part of these amounts probably originates in the adrenal glands The sudden appearance at puberty of the secondary sex characters is due to an increased responsiveness on the part of the tissues to androgen. During sexual maturity the androgens maintain the sex characters The androgen output again declines with advancing age. Spermatogenesis, however, may continue to an advanced age. Spermatogenesis is dependent on a mutual interrelation of pituitary-gonadotropic and testicular-androgenic activity

17-Ketosteroids The known metabolites of testosterone are included in the group of compounds known as the neutral (to distinguish them from estrogenic phenols) 17-ketosteroids The androgen excreted in the urine differs in many respects from that extracted from testes It consists principally of androsterone, which is a 17-ketosteroid body

Normally about 15 mg of ketosteroid bodies are excreted in the urine daily by an adult. Of this amount about 9 mg. are derived from the adrenals, the remainder from the testes After testicular atrophy a considerable fraction of these ketosteroids remains. Since pituitary insufficiency induces both testicular and adrenocortical insufficiency, however, 17-ketosteroid bodies disappear from the urine in this condition In severe adrenocortical insufficiency the excretion falls to about 5 mg daily There is an increase in 17-ketosteroid excretion in Cushing's syndrome and in adrenocortical hyperactivity.

Pubescence. The onset of pubescence varies in normal boys from 10 to 16 years of age, and in rare isolated cases may begin even later Most prepubescents manifesting small genitalia, excessive obesity or similar disturbances often attributed to endocrine deficiency grow into normal adults and require only an adequate diet and the usual hygienic measures to insure their normal development It is important to be aware that sexual development beginning in girls aged less than 8 years and boys aged less than 10 years requires explanation if such can be had by examinations and the family history These studies will usually reveal that about 9 of every 10 cases of sexual precocity are due to pituitary activation by unknown causes Sexual precocity due to intracranial tumor runs a rapidly fatal course and is commoner in girls than in boys. However, pineal tumors are commoner in boys than in girls.

While there are essential statistical differences in the anthropologic measurements of the somatic diameters of the male and female bodies, it is essential to realize that these differences may not denote abnormalities in body shapes, sizes and functions. The rough, strong, visibly breastless woman with some beard, large feet and hands, and long straight legs and arms may bear children as well as, if not better than, her delicately contoured sister In the extremes of normal limits, therefore, the main differences between men and women which are termed secondary sex characteristics are statistical figures and do not indicate functional performances The early development of a body type is more attributable to heredity than to the influence of gonadal hormones.

Male Hypogonadism (Eunuchoidism). *Failure of testicular function* and deficiency of the male hormone give rise to varying degrees of eunuchoidism or, in some, to the same symptoms that follow castration.

and women. Those of the second group occur in the body fluids of pregnant women and their detection is the basis of the Aschheim-Zondek, Friedman and frog tests for pregnancy. These same gonadotropic hormones exist in greatly increased amount in the presence of pathologically proliferating chorionic tissue, such as hydatid mole, chorion-epithelioma, and in some tumors of the testicle

The *pituitary hormones* have not been isolated in pure form. Their presence is detected by biologic reactions and changes in the generative tract. The pituitary gland elaborates two gonadotropic hormones which have to do particularly with ovarian functions One stimulates the growth of the graafian follicle up to the time of maturation of the ovum and ovulation. This hormone is designated as the follicle-stimulating hormone. The other gonadotropic hormone has the function of luteinization of the follicle and thus produces the corpus luteum with the formation of progesterone. A third anterior pituitary hormone is luteotrophin, formerly known as prolactin In addition to its influence on the breasts it initiates and maintains the secretory activity of the corpus luteum (see p 1105).

Progesterone is a derivative of androstene The chief metabolite of progesterone is pregnane, which occurs in relatively large amounts in the urine during pregnancy The name pregnanediol is often used instead of progesterone Steroids of the progesterone group have been isolated from the adrenal glands and recovered from the urine of castrates of both sexes

As has been stated in the description of testicular hormones, small amounts of gonadotropic substance are found in the urine of both men and women, irrespective of age. Since this substance is present in greatest concentration after the menopause or castration, it is called the *hormone of castrate urine* to distinguish it from the hormone of pregnancy urine (see p. 1115)

Tests for Pregnancy. The urine of pregnant women contains a gonadotropic substance which is the basis of the urinary test for pregnancy In the mammals the intravenous injection of a few milliliters of the urine of a pregnant woman will cause the formation of hemorrhagic and ruptured follicles in 48 hours, the test is accurate in more than 90 per cent of cases The hormone is detected by its action on the ovaries of rats, mice (Aschheim-Zondek test), rabbits (Friedman test), and frogs (Hogben or xenopus test).

In the Hogben pregnancy test the South African clawed toad (*Xenopus laevis*), an animal that carries eggs at all times of the year but extrudes them only after coitus or after injection of gonadotropins, is utilized The injection (subcutaneous or into the dorsal lymph sac) of a suitably prepared extract of the urine of a pregnant woman is followed by the extrusion of eggs in from 4 to 6 hours These can be seen by the naked eye

The Hogben test is more rapid than the Friedman and the Aschheim-Zondek tests and is preferred by many gynecologists However, it is not reliable before the fortieth day of pregnancy and this limits its use

If the urine continues to show a high content of gonadotropic hormone after the termination of a normal pregnancy, or after operation for tubal pregnancy or curettage for incomplete abortion, the presence of hydatid mole or chorionepithelioma is strongly suspected The continued high titer of this hormone in cases of hydatid mole, chorion-epithelioma, or testicular tumor indicates that these growths have not been destroyed or removed, they are progressing either locally or by metastasis.

The Estrogenic Hormones. The ovarian control of the reproductive function and secondary sex characteristics is mediated by the ovarian hormones, estrogen and progesterone. The estrogen is produced by the graafian follicle, and the progesterone by the corpus luteum.

Estrogen is the growth hormone, stimulating the growth of the uterus, uterine tubes, vagina, and mammary glands, controlling the development of secondary sex characteristics, and presiding over the regeneration of the endometrium after each menstrual period From the influence of estrogen the female acquires sexual maturity, and conception and reproduction may be assured

Estrogens are elaborated by the ovaries for the most part during the first 2 weeks of the menstrual cycle and are inhibited by the action of progesterone during the rest

ł. In these there is an elevation of gonadotropic excretion in the urine com-
le with that observed in castrates, and histologic examination of the testes
s signs of atrophy or degeneration of the interstitial tissue. The intramuscular
iistration of 25 mg. of testosterone propionate for 5 days weekly for 2 weeks
ɔe used as a therapeutic test, with proper consideration of the possibility that
ɔserved effects may be due to suggestion.

the treatment of the male climacteric methyl testosterone in doses of 30 to
; daily sometimes is administered orally Such treatment is of no value.

ale Hypergonadism. Overproduction of the endocrine secretion of the testes
adult gives no symptoms attributable to an excess of the hormone The abnor-
exual urge observed in men who have criminal tendencies is not due to any
oduction of male hormone but is the result of some psychiatric abnormality,
ius these men may be unaffected by castration.

ypergonadism prior to puberty leads to precocious development. Interstitial
mors of the testes may secrete an excess of the male hormone in boys which
; the premature development of the secondary sex characters and in some
induces skeletal and muscular development This condition is rare, for most
ces of precocious sexual activity in the male are induced by abnormalities in
pothalamus, or pineal region of the brain By stimulating the testes, which
ie prematurely active, these affections of the nervous system give rise to true
l precocity with spermatogenesis Androgenic tumors of the adrenal occur
arely in boys and are not accompanied by spermatogenic activity

omosexuality. Homosexuality is a sexual perversion and not an endocrine
ɔance However, it has been attributed to a hormonal imbalance since some
exuals show eunuchoidal characters Many homosexuals are affected by hypo-
ism, which some have generously conceded might be, in part, responsible for
ndition In practice, however, the gonads and secondary sex characters of
iomosexuals are found to be normal. In each homosexual it is necessary to
ɔt an evaluation of the relative effects of psychogenic, acquired and endocrine
; in the pathogenesis of the disorder. There are often, however, a relative
se in estrogen and a decrease in the androgen content of the urine

ychiatric rather than endocrine therapy is the better form of treatment

e Female Sex Hormones. In the female, as in the male, endocrine glands
volved in the process of sexual maturation In women these are the ovaries and
yroid, parathyroid, adrenal and pituitary glands A failure of proper function
one of these in its development or activity may result in inadequate genital
pment or in irregularity of or no menstruation

xual maturity exists from adolescence until the menopause This period of
30 years is marked by the regular sequence of ovulation and menstruation
y the ability to conceive and reproduce If the hypophysis or the ovaries are
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the menopause the reproductive propensities cease, and during *this period*
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uterus, ovaries and vagina

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e Gonadotropic Hormones in the Female. *The gonadotropic* hormones in the
; are concerned with development of the reproductive ducts, the formation of ova,
uation, and the processes that make reproduction possible.

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are derived from the pituitary and occur in the blood and urine of normal men

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of the time. It is during the first 2 weeks of the cycle that the uterine muscle exhibits the greatest cyclic changes in motility. The increased motility is at its height during the period of follicular growth, it decreases during the last 2 weeks, under the influence of progesterone. Uterine motility is distinctly sluggish during the first trimester of pregnancy, as long as the corpus luteum exerts a controlling influence.

At the beginning of each menstrual cycle many immature follicles develop but only one or two reach full maturity. The rest degenerate. A single graafian follicle will not mature normally if smaller follicles are not present.

Within 5 or 6 days after the endometrium is cast off during menstruation, it is regenerated. This is the result of the natural tendency of tissue to heal This process may be stimulated and accelerated by estrogen

It is known that large amounts of estrogen are formed and excreted during pregnancy. The administration of large doses of estrogen early in pregnancy may cause nidation of the fertilized egg or later abortion or congenital malformation.

Hyperstimulation with estrogens after the menopause may produce endometrial hyperplasia and uterine bleeding similar to that caused by certain ovarian tumors after the menopause.

The Corpus Luteum Hormones. A function of the corpus luteum hormone, *progesterone*, is the preparation of the endometrium for the nidation and nourishment of the fertilized ovum The endometrium is sensitized so that, in the presence of the embryo, it forms the maternal part of the placenta, the decidua The corpus luteum inhibits uterine motility in both the pregnant and the nonpregnant uterus

The menses can be suppressed by the use of progestin or progesterone or stilbestrol. Progestin also is a substitute for the ovarian secretions in maintaining pregnancy.

The corpus luteum seems to have no useful action except in either preparing the uterus for pregnancy or enabling the gestation to continue. Progesterone is not necessary for the health of the individual, likewise the administration of progesterone has not been followed by any harmful effects in either human beings or animals

Pregnanediol is the end product in the metabolism of progesterone and is derived from it Pregnanediol appears in the urine a day or two after ovulation. The excretion becomes greatest about a week before menstruation and usually disappears entirely 2 or 3 days before the onset of bleeding The curve of excretion of pregnanediol thus parallels the life history of the corpus luteum

Relaxin is a hormone secreted by the corpus luteum but its significance is not known

The Controls of Ovulation. Menstruation is generally accepted as an indication of ovarian function

Endocrine disorders such as dysfunction and diseases of the pituitary, thyroid and adrenal glands, and primary ovarian failure may prevent ovulation These disturbances also may stop normal female sexual function and impose masculine features Destructive diseases such as tuberculosis, tubo-ovarian abscess, or neoplasms may damage the ovarian cortex so severely that ovarian function is eliminated Ovarian damage by surgical operations or pathologic processes which disturb the blood supply of an ovary may cause it to become cystic If the ovary is injured sufficiently, menopausal symptoms develop

[illegible] functioning
[illegible] that ovula-
[illegible] However,

menstrual function or ovulation is extremely susceptible to external stimuli In the midst of a normal menstrual period the flow may be stopped abruptly by physical or psychic shock, or by getting chilled or fatigued Some young women may stop menstruating for months without any known cause Menstruation ceases during the course of many acute or chronic infections such as pulmonary tuberculosis or severe fevers, and in idiopathic ulcerative colitis or ileitis. The mode of action of such stimuli on ovulation is unknown Inhibition of ovulation by progesterone is the cause of nonovulation during pregnancy In rare instances a woman may menstruate without ovulation, or she may ovulate without menstruating Ovulation without menstruating occurs during the puerperium.

The Time of Ovulation; the "Safe Period." Ovulation normally occurs between menstrual periods. The commonest date is approximately between the eleventh and fourteenth days.

In recent years it has been taught by some that sexual intercourse may be practiced without fear of pregnancy and without the use of contraceptives during approximately the 2 weeks prior to the oncoming menstrual period This period has been designated the safe period. Physicians realize the uncertainty of such advice, for many women ovulate irregularly, and the practice of the safe period for them is often disappointing. Those who must use this method of contraception and who do not know when they ovulate may be told that the usual period of fertility extends from the eleventh to perhaps the fifteenth day of the cycle, at other times the likelihood of conception is more remote.

Periodic Intermenstrual Pain (Mittelschmerz). Periodic intermenstrual pain is usually limited to young women less than 30 years old It is characterized by a regular periodicity of the pain, occurring always the same number of days after menstruation. There is pain in the suprapubic region, in one or both iliac fossae Commonly it is diffuse through the whole pelvis and is said to resemble the pain of dysmenorrhea or very mild labor pain Some have the pain in the right and left sides alternately on successive months In some women the pain is severe and incapacitating and is followed by soreness and nervousness until the next menstrual period. In these cases the symptoms often simulate those of acute appendicitis or salpingitis A painful ovulation associated with severe intra-abdominal bleeding from the ruptured ovary is rare. Associated vaginal bleeding may be enough to be noticed by the patient and to require some protection

If the examination is made at a time when there is no discomfort, when the patient is not ovulating, the palpatory examination in cases of ovulatory pain may reveal nothing at all If the patient is examined while she is in the midst of ovulatory pain, there will be tenderness through the whole pelvis, the cul-de-sac, and both fornices

Without internal hemorrhage there is no leukocytosis In the presence of hemorrhage the leukocyte count may be very high, 15,000 to 25,000 per cubic millimeter.

The temperature drops just before the date of ovulation and then rises perhaps 1 F near the time of actual rupture of the follicle

The [illegible] In cases with abdominal bleedin [illegible]
extra-u [illegible]
sources, and other acute pelvic conditions

Menstruation. The ovarian hormones estrogen and progesterone are the direct controls of menstruation. The indirect control is vested in other glands of internal secretion. As has been stated, there are ovulatory and anovulatory menstruations

In *ovulatory menstruation* ovulation occurs during the menstrual cycle, with the formation of the corpus luteum and the consequent production of progestational reaction in the endometrium The bleeding is from a progestational endometrium

The length of the menstrual cycle, if measured from the first day of menstrual flow, averages about 28 days Variations up to 4 or 5 days are present in most women. Many women menstruate habitually at intervals of from 21 to 23 days, others every 35 or 40 days

The loss of blood during menstruation varies (average 50 mg. of iron) tremendously with individual women and from month to month in the same person. It is important to realize that a fairly constant amount of blood is lost during each period by a given woman, and that wide variations in the amount of blood lost are compatible with normal health and the reproductive function. Women generally can fairly accurately estimate the blood loss by the number of napkins they use per day The normal woman does not get up and change napkins at night.

of the time It is during the first 2 weeks of the cycle that the uterine muscle exhibits the greatest cyclic changes in motility. The increased motility is at its height during the period of follicular growth, it decreases during the last 2 weeks, under the influence of progesterone Uterine motility is distinctly sluggish during the first trimester of pregnancy, as long as the corpus luteum exerts a controlling influence.

At the beginning of each menstrual cycle *many immature follicles develop but only* one or two reach full maturity. The rest degenerate. A single graafian follicle will not mature normally if smaller follicles are not present.

Within 5 or 6 days after the endometrium is cast off during menstruation, it is regenerated This is the result of the natural tendency of tissue to heal. This process may be stimulated and accelerated by estrogen

It is known that large amounts of estrogen are formed and excreted during pregnancy. The administration of large doses of estrogen early in pregnancy may cause nidation of the fertilized egg or later abortion or congenital malformation.

Hyperstimulation with estrogens after the menopause may produce endometrial hyperplasia and uterine bleeding similar to that caused by certain ovarian tumors after the menopause

The Corpus Luteum Hormones. A function of the corpus luteum hormone, *progesterone,* is the preparation of the endometrium for the nidation and nourishment of the fertilized ovum The endometrium is sensitized so that, in the presence of the embryo, it forms the maternal part of the placenta, the decidua The corpus luteum inhibits uterine motility in both the pregnant and the nonpregnant uterus.

The menses can be suppressed by the use of progestin or progesterone or stilbestrol Progestin also is a substitute for the ovarian secretions in maintaining pregnancy.

The corpus luteum seems to have no useful action except in either preparing the uterus for pregnancy or enabling the gestation to continue. Progesterone is not necessary for the health of the individual, likewise the administration of progesterone has not been followed by any harmful effects in either human beings or animals

Pregnanediol is the end product in the metabolism of progesterone and is derived from it Pregnanediol appears in the urine a day or two after ovulation The excretion becomes greatest about a week before menstruation and usually disappears entirely 2 or 3 days before the onset of bleeding The curve of excretion of pregnanediol thus parallels the life history of the corpus luteum

Relaxin is a hormone secreted by the corpus luteum but its significance is not known

The Controls of Ovulation. Menstruation is generally accepted as an indication of ovarian function

Endocrine disorders such as dysfunction and diseases of the pituitary, thyroid and adrenal glands, and primary ovarian failure may prevent ovulation These disturbances also may stop normal female sexual function and impose masculine features Destructive diseases such as tuberculosis, tubo-ovarian abscess, or neoplasms may damage the ovarian cortex so severely that ovarian function is eliminated Ovarian damage by surgical operations or pathologic processes which disturb the blood supply of an ovary may cause it to become cystic. If the ovary is injured sufficiently, menopausal symptoms develop

It may be stated, then, that ovulation is controlled by a synchronized functioning of the pituitary gland and the ovary or ovaries Generally the indication that ovulation is proceeding normally is the cyclic appearance of the menstrual flow However, menstrual function or ovulation is extremely susceptible to external *stimuli In the* midst of a normal menstrual period the flow may be stopped abruptly by *physical* or psychic shock, or by getting chilled or fatigued Some young women may stop menstruating for months without any known cause Menstruation ceases during the course of many acute or chronic infections such as pulmonary tuberculosis or severe fevers, and in idiopathic ulcerative colitis or ileitis The mode of action *of such stimuli* on ovulation is unknown Inhibition of ovulation by progesterone is the cause of nonovulation during pregnancy. In rare instances a woman may *menstruate* without ovulation, or she may ovulate without menstruating. Ovulation without menstruating occurs during the puerperium

Cryptomenorrhea may occur in the ectopic endometrium in the ovary or elsewhere. In these cases of endometriosis menstrual blood is retained in the ovary, forming a hemorrhagic cyst, or collects in the pelvis to form a pelvic hematocele. If the cervical canal is occluded by operative scar, malignant lesion, or childbirth injury, the menstrual blood collects in the uterus (hematometra) or in the uterine tube (hematosalpinx). If there is an imperforate hymen, the menstrual fluids collect in the vagina (hematocolpos) and may be forced back into the uterus, uterine tubes, and pelvic cavity.

The presence of amenorrhea without organic disease has been attributed to psychic or physical shock. Amenorrhea in association with pulmonary tuberculosis, diabetes, heart disease and serious intestinal diseases is common Diseases of the endocrine glands are rare causes of amenorrhea

In *menorrhagia* there is not only an increase in the amount of flow, but often also a prolongation of the flow occurring at the regular menstrual time Menorrhagia is one of the commonest menstrual disorders of adolescence and the menopause, it is a cardinal symptom of endometrial hyperplasia Menorrhagia is often a symptom of uterine myomas, endometriosis, salpingitis, chronic subinvolution of the uterus, endometritis, retained placental tissue, uterine cancer, and pelvic tumors.

Metrorrhagia is found in a variety of conditions cervical polyp, myoma of the uterus, retained placenta, ovarian tumors, vaginal lesions, prolapse of the uterus with cervical ulceration, tubal pregnancy, hydatid mole, and occasionally in the rare condition of malignant disease of the uterus, and in other conditions It is also found in functional disorders, especially hyperplasia of the endometrium

Direct trauma or *laceration* of the genitals produces vaginal bleeding. After automobile accidents or falls there may be severe uterine bleeding, without any visible injury to the cervix, uterus, or external genitals The cause is not always clear. It may be due to rupture or injury to the graafian follicle or corpus luteum, which would be followed by uterine bleeding In such cases an abortion is always to be suspected.

In the presence of abnormal menstruation, and occasionally in the presence of normal menstruation, more specific data in regard to ovarian functions may be necessary for diagnosis. These data are obtained by several different methods By *endometrial biopsy* the competent pathologist can diagnose the presence of a functioning corpus luteum or determine whether follicular development is normal

Vaginal bleeding during ovulation is rare Microscopic vaginal bleeding, however, is not uncommon, and with these small amounts of vaginal bleeding during ovulation may be an accompanying observable increase in the amount of leukorrhea and also vague discomforts in the pelvic area (Mittelschmerz)

Vicarious menstruation perhaps occurs in some patients who do not menstruate normally but who have an ample production of the estrogenic hormone. Often there is rhinorrhea and other nasal symptoms and at times epistaxis occurring at the time of the menstrual bleeding Perhaps there is a relationship between genital stimuli, activity of the breasts and of the genital spots of the nasal mucosa. Vicarious menstruation is alleged to occur more frequently from the nose or the breasts.

MENSTRUAL IRREGULARITIES. Menstrual irregularities or functional uterine bleeding occurs most frequently in adolescence, and in this period all menstrual irregularities are considered to be of functional origin until they are proved otherwise In the *period of sexual activity functional* irregularities constitute one fifth of all causes of abnormal uterine bleeding

In the menopausal years menstrual irregularities are again frequent However, all irregular uterine bleeding which occurs during the menopause is considered to be due to organic diseases until proved otherwise

The menstrual period is often preceded and followed by a moderate, mucoid leukorrhea. The breasts often enlarge and become painful.

All normal nonneurotic women regard menstruation as an unavoidable inconvenience; only a small minority are incapacitated by it.

In *ovulatory menstruation* the endometrial changes during the *menstrual cycle* may be divided into four phases· proliferative, secretory, premenstrual regression and menstrual desquamation.

The proliferative phase begins with the end of the menstrual flow and extends to the time of ovulation This is the period of estrogenic stimulation, and at this time *the graafian follicle is ripening in the ovary*

The secretory phase extends from the time of ovulation until the regression of the corpus luteum During this phase the corpus luteum runs its active course, the endometrial growth is brought about by the secretion of the corpus luteum, progesterone

The premenstrual phase lasts for 2 or 3 days, beginning shortly after the degeneration of the corpus luteum and ending with the onset of menstrual flow.

The phase of desquamation is the period of menstrual bleeding

Anovulatory menstruation may be defined as a form of menstruation which is characterized by the lack of ovulation and the consequent absence of corpus luteum formation There is no secretory stage of endometrial growth, and the bleeding occurs from an endometrium that shows only the follicular stimulation. Anovulatory menstruation is therefore periodic uterine bleeding. The gross characteristic of anovulatory menstruation is a greater loss of blood

Possibly 1 woman in 12 may menstruate from an endometrium that shows no influence of corpus luteum Perhaps 1 in every 20 of all menstrual periods in healthy women with normal menstrual histories is an anovulatory menstruation

Anovulatory menstruation is observed more frequently in women who have obesity, endocrine disorders, and metabolic disorders produced by many conditions In these women ovarian function may be seriously disturbed for prolonged periods of time, and sterility is particularly common

Anovulatory menstruation is determined by biopsy of the endometrium obtained within 1 or 2 days before a menstrual period or on the first day of the flow. A proliferative type of endometrium at this period shows no progestational (corpus luteum) influence, and therefore it is concluded that the menstrual period is anovulatory

Precocious menstruation is associated with (1) adrenal tumors, (2) ovarian tumors, (3) lesions of the brain and (4) lack of any demonstrable pathologic lesion. This is not a true development of the reproductive organs but rather a false, precocious stimulation of certain elements in the reproductive organs, simulating a true growth The largest group of young girls who have precocious menstruation have no demonstrable disease

The average age at occurrence of the menarche is between 13 and 14 years, there is a wide normal variation, with ranges between 10 and 18 years *Heredity*, diet, climate, race, health and other factors all play a part

MENSTRUAL DISORDERS. Menstrual disorders and irregular uterine bleeding occur at all ages but most frequently during adolescence and the menopause (functional uterine bleeding)

Amenorrhea or complete absence of menstruation may develop suddenly, or it may be preceded by a gradual decrease in the amount of menstrual flow (oligomenorrhea), or decrease in the frequency of menstruation. Hidden or retained *menstruation* (cryptomenorrhea) is always to be considered in those who are of the correct age and do not have manifest periods. However, the occurrence of cryptomenorrhea is rare.

symptom of many gynecologic disorders. As a rule, any pelvic discomfort is exaggerated by menstruation.

Ovarian Hypogonadism. Subnormal endocrine activity of the ovaries, like that of the testes, cannot be judged by the patient

Ovarian deprivation is manifested by the asexual features of girls before puberty and changes that occur at the menopause or after the removal or inactivation of the ovaries during the period in which reproduction is possible The effects differ, depending on the age at which ovarian function is terminated and on the health of the ovaries at the time they are removed Before puberty, loss of ovarian function is followed by sexual infantilism, which is approximated in instances of ovarian failure due to hypopituitarism in adolescence and in follicular agenesis. During sexual maturity the characteristic changes that follow bilateral oophorectomy with the consequent loss of estrogenic substances in a young, sexually active woman are amenorrhea, hot flushes, nervousness, loss of libido, gain in weight, insomnia, and other nervous reactions. These are the symptoms of the menopause and they may appear whether the ovarian function is eliminated by bilateral oophorectomy, irradiation, disease, or normal processes which occur at the climacteric

The processes by which the young girl may be deprived of all or a part of the endocrine functions of the ovaries are many Some of these processes may be enumerated: agenesis of the ovaries, misplacement and degeneration of the ovaries in the inguinal canals, cystic degeneration and inflammatory disease Dysfunction of the ovaries may result from dysfunction of the pituitary or the thyroid gland, malnutrition, chronic disease, or toxic conditions and from indeterminate causes

In ovarian infantilism, at puberty the secondary sex organs and characteristics fail to develop. The uterus, vagina, and uterine tubes remain infantile The growth is greatly retarded

Ovarian eunuchoidism, in contrast to ovarian infantilism, is characterized by accentuation of growth due to delayed closure of the epiphyses with a disproportion in the length of the upper and lower extremities As in infantilism the secondary sex organs and characteristics do not develop

Menopause. *The menopause* is termed *induced* or *artificial* if it is brought on by surgical operation or irradiation It is *premature* if it occurs at an early age, and is *delayed* if menstruation continues past the usual age for menstruation

Amenorrhea follows the cessation of ovarian activity and production of estrogen However, estrogen continues to be produced somewhere in the body Menopausal amenorrhea may come on gradually; it may be preceded by a decrease in the amount of flow for a year or more. During this time occasional periods may be missed Finally amenorrhea is permanent and complete In other women the menses cease abruptly and permanently. Occasionally, months after the patient has had her last menstrual period, there may be a recurrence of bleeding for a few days Often this is due to endocrine therapy.

The age at the appearance of the menopause is inheritable The average age for the menopause is from 45 to 50 years Some women may menstruate till they approach 60. An occasional woman menstruates past the age of 60 years The menopause may also occur without apparent cause at almost any age after onset of menstruation

True menopausal symptoms include vasomotor disturbances, hot flushes, nerv-

of organic disturbances.

Some women never have hot flushes, others are made miserable by them As a rule, they make their appearance before the amenorrhea is fully established, are fairly frequent and annoying for 6 months or a year, and then gradually or rapidly

Irregular or functional uterine bleeding can come from any type of endome including normal estrogenic or proliferative; hyperestrogenic or hyperplastic; n progestational, atrophic (castrate or postmenopausal type); or mixed variet endometria.

The pelvic organs are often palpably normal in functional bleeding. In th vanced age groups normal size of internal genitalia may not be a safe criteri the health of these organs.

In some instances of menstrual irregularities endometrial studies are rec for diagnosis Adequate endometrial studies include examination, by a comp pathologist, of a specimen taken on the first day of the menstrual flow or just b menstruation, to include the progestational phase. The finding of progesta endometrium in many women who have functional bleeding suggests that la ovulation and deficient corpus luteum function may not always cause this ir larity.

The pathologist will often report the presence of *endometrial hyperplasia studies of uterine tissue removed by curettage In some instances of functional u* bleeding hyperplasia of the endometrium, due primarily to the stimulation by e gen, is present Endometrial hyperplasia often occurs in women approachin menopause. It occurs also, however, after the menopause and in infants Its o rence after the menopause may in some instances be due to the administrati estrogen or to ovarian tumor.

Excessive and prolonged menstruation is the characteristic symptom of h plasia. The menstrual flow may be so prolonged that it is practically contin After the menopause hyperplasia may be manifested by vaginal bleeding

The clinical significance of the diagnosis of hyperplasia varies with the a the patient In puberty hyperplasia is usually uncomplicated, and curettage erally confers relief from the irregular bleeding In the period of sexual mat associated pathologic lesions are commonly found, hence the hyperplasia is always to be accepted as the sole cause of bleeding. In the postmenopausal y a malignant lesion accompanies hyperplasia in almost one third of the cases Hy plasia as the final explanation of postmenopausal bleeding is not acceptable u malignant disease has been excluded by repeated examinations over a prolo period of time.

In adult and aged women who have functional uterine bleeding, if the resul physical examination are negative, curettage and biopsy of the cervix are neces If these and other examinations reveal nothing abnormal, the bleeding is tentati accepted as functional but not definitely diagnosed as such until sufficient time (eral months) has elapsed to prove that organic disease is not present. In adoles girls functional bleeding is the rule, and treatment for the condition is gene not advisable Maturity and not gestation may cure functional uterine bleedin girls. In the presence of diseases of the blood such as purpura, pernicious ane and leukemia, uterine bleeding may be serious

Dysmenorrhea (painful menstruation) is termed primary when it is not ass ated with any demonstrable pathologic disorder; it is designated as secondary w it is accompanied by organic gynecologic disease

In *primary dysmenorrhea* often the first few menses after the menarche normal. Pain ensues irregularly The degree of pain varies, and is described ... In severe dysmenorrhea the pain is present s

to these women that as they get ol

Secondary dysmenorrhea by definition is associated with organic pelvic dise It may not date from the onset of the pelvic disease, for many have always had In those who do not have a history of dysmenorrhea this symptom may then app after or during the course of some pelvic disease. Secondary dysmenorrhea

The Endocrine Assays Correlated With Clinical Manifestations Which Are Helpful in Diagnosis. The gonadotropin-follicle stimulating hormone is *increased* after the menopause, after castration, and in the presence of primary hypogonadism such as ovarian agenesis and secondarily in the presence of degeneration of the seminiferous tubules and tumors of the Leydig cells of the testicles. The gonadotropin-follicle stimulating hormone is *decreased* in pituitary infantilism, in anorexia nervosa, in the presence of profound psychoneurosis and in some psychoses This hormone is present in insignificant amounts or absent before puberty.

The chorionic gonadotropic hormone is *increased* during pregnancy and in the presence of chorionepithelioma and hydatiform moles.

Androgens or 17-ketosteroids which have a dual source of origin in the male—the adrenal cortex and the testicles—are *increased* in the adrenogenital syndrome, in adrenal tumors and in Cushing's syndrome due to cortical hyperplasia or carcinoma. In the presence of adenoma of the adrenal cortex when the contralateral adrenal is hypertrophied, the concentrations of 17-ketosteroids may be decreased In sexual precocity due to a hormone-producing tumor of the testicle, the 17-ketosteroids are increased In sexual precocity due to neurogenic or constitutional causes the 17-ketosteroids have normal values The 17-ketosteroids are *decreased* in Addison's disease, pituitary infantilism, primary hypogonadism, ovarian agenesis and testicular tubular degeneration

The adrenal glycogenic factor or neutral reducing lipids are *increased* in Cushing's syndrome and *decreased* in Addison's disease. The concentration of this substance is tested for by employment of sugar tolerance tests: response to insulin and ACTH Small doses of 5 to 10 units of insulin may cause hypoglycemia. The administration of ACTH, in the presence of reduced concentrations of the adrenal glycogenetic factor, causes an increase in the eosinophils in the circulating blood, increased excretion of uric acid and an increase of 17-ketosteroids in the urine

The adrenal electrolyte factor is occasionally *increased* in Cushing's syndrome. It is *decreased* in Addison's disease Its concentration is implied by determinations of the serum sodium, potassium and chloride and by the amount of carbon dioxide of the blood It may also be inferred by the results of the diuresis test of Kepler, Robinson and Power

The adrenal medulla or pressor factor (epinephrine and norepinephrine) is increased in the presence of the following tumors of the adrenal medulla sympathogonioma, neuroblastoma, ganglioneuroma and pheochromocytoma. The common tests employed for detection of excessive amounts of epinephrine and norepinephrine are the benzodioxane and the histamine tests.

The posterior pituitary and hypothalamic area may fail to produce adequate amounts of the antidiuretic factor and as a consequence diabetes insipidus may ensue. This condition is indicated by the consistent passage of urine with a specific gravity which is always less than 1 005

The estrogens are *increased* in the presence of pregnancy, granulosa or thecal cell tumor of the ovary, chorionepithelioma and some adrenal cortical tumors and hyperplasias Estrogens are *decreased* in sexual infantilism of either pituitary or ovarian origin and amenorrhea

Estrogenic excesses and deficiencies are often determined by a study of the vaginal smear, vaginal or endometrial biopsy and the histologic study of estrogen-producing tumors

Progestin is *increased* in the presence of pregnancy, luteoma of the ovary and some adrenal tumors It is *decreased* in the presence of anovulatory menstrual cycles. Excessive amounts are determined by a study of the basal temperature, vaginal smear and endometrial biopsy

disappear. They may be present in varying degree for 1 to 3 years. They may according to the history, 10, 20, or even 25 years A suspicion should alway aroused that in these instances of prolonged hot flushes there may be a desire of complainant to impress the "girls" with her youth.

The amount of inconvenience that a woman suffers depends largely on her attitude toward discomfort, her fortitude and mental stability The sudden depr tion of ovarian function precipitates a more marked menopausal reaction t occurs in the natural course of events Hot flushes after simple hysterectomy du menstrual life result from operative or postoperative injury or diseased ovaries

The postmenopausal ovary contains no follicles It seems to have no func whatever after the menopause, and its removal after that event causes no sympt of endocrine deprivation or imbalance

After the menopause the uterus becomes smaller, the endometrium inact thin, and atrophic The vaginal epithelium becomes very thin, not more than a th or quarter as thick as in normal sexual life The external genitalia become smal flabby, and lose *their subcutaneous fat and elastic tissue. The breasts atrophy.*

In the vagina the atrophy of the epithelium is accompanied by a decrease glycogen content, and the secretions become neutral or alkaline. After the me pause senile vaginitis is common and is manifested by irritation of the vaginal w which may lead to cicatricial constriction and eventual obliteration of the up part of the vagina. This senile irritation is benefited by the use of vaginal suppo tories containing estrogens

There is an increase in the amount of gonadotropins in the blood and uri

Postmenopausal Bleeding. Malignant disease is the cause of postmenopau bleeding in 6 of every 10 who have it. The commonest single cause of postmer pausal bleeding is cervical polyp Cancer of the cervix is next in importance Oth *causes are carcinoma of the uterine body, uterine prolapse with ulceration of t* cervix, ovarian tumors, endometrial polyp, and senile vaginitis There are numero other causes, a few of which are sarcoma of the endometrium, sarcoma in myom *chronic endometritis, hyperplasia of the endometrium,* ulceration from a vagin pessary, urethral caruncle, urethral prolapse, and primary vaginal malignant d ease, including metastatic tumors of the vagina. There will remain a number patients in whom no cause is revealed by curettage, biopsy, or pelvic examinati by physical means.

In a few patients diagnosis of postmenopausal bleeding *is established by exam* ination by physical means. The cause can be seen or felt When this is impossibl curettage is required. If the foregoing procedures do not reveal the cause, it *situated in the uterine wall, or in an inaccessible part of the endometrium,* or the adnexa In these cases the pelvis should be explored through a laparotomy.

Ovarian Hypergonadism (*Precocious Puberty*). Ovarian hypergonadism ca not be determined from the history Nymphomania is of psychic and not of endo crine origin.

The definite form of ovarian hypergonadism (*precocious puberty*) is encoun tered in childhood. In some girls early in childhood the secondary sex organs an characteristics develop and ovulation and menstruation proceed normally. Ther *is no evidence of tumors or abnormalities in the ovaries* or any of the ductles glands. This condition may be caused by disease of the hypothalamus, encephaliti or polyostotic fibrous dysplasia

There is an early closure of the epiphyses The bone age as revealed by roent genograms is several years in advance of the chronologic age.

Precocious puberty or ovarian hypergonadism *is differentiated* from that result ing from ovarian tumors because ovulation does not occur in the latter; and from adrenal tumors because true precociousness does not occur *as a result of these* tumors.

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15

SOME DISORDERS INVOLVING THE CRANIAL PORTION OF THE CENTRAL NERVOUS SYSTEM

The descriptions of the diseases of the nervous system which follow are limited to the diseases of the cranial portion of the central nervous system The diseases of the spinal cord and the peripheral nerves and their association with the cranial portion of the central nervous system have been considered in connection with the locomotor system

The complexities of the central nervous system require knowledge of its structure and function in order to determine within it the localization of disease The diagnostic difficulties are increased because there are many parts of the system to which definite function or functions cannot be assigned. In the discussion of diseases of the nervous system which follows, it is hoped that the brevity of discussion will not be interpreted as implying that the diagnosis of disease of this system is always easy or that it can be quickly accomplished Diagnosis of disease of the central nervous system, with any degree of accuracy, requires the constant daily application of knowledge of neuro-anatomy and neurophysiology not possessed by those who have not had special training in this field of endeavor Even if special training has been received, proficiency in diagnosis cannot be maintained unless this training is in constant use

CONGENITAL AND HEREDITARY DISEASES OF THE NERVOUS SYSTEM

The terms congenital and prenatal are synonymous There are the prenatal diseases of the nervous system which arise or begin during intra-uterine life and those which are due to morbid heredity, for instance those which are passed along in the germ plasm Sometimes prenatal and hereditary diseases can be separated, and at other times separation and assignment to one or the other category is impossible.

In regard to intra-uterine causes for prenatal disease, it seems that defects of development may result from transient disturbances of embryonic metabolism possibly caused by defective implantation or infarction of the placenta and maternal toxemias Little is known about placental disorders and the destruction of parts of the nervous system during intra-uterine life. Some infections, such as toxoplasmosis, German measles and syphilis, of the mother may be transmitted to or their toxins may reach the fetus in utero. Roentgenotherapy of the pelvis during pregnancy may cause defects of the nervous system in the fetus. It may be difficult, however, to prove that the roentgenotherapy caused a particular defect.

Hereditary disease of the nervous system may be manifest at birth, and there often is a history of similar defects in relatives. If the disease is not manifest at birth, and occurs later in life, there should be no evidence of postnatal disease of the nervous system occurring during infancy which could account for the affliction if the disease is to be attributed to prenatal influences. However, a symptom-free

interval following birth is not against the diagnosis of defective development of the suprasegmental structures, for functions of these structures become evident as age advances Characteristically, a hereditarily defective nervous system reacts excessively to mild birth trauma, infections, and disturbances of nutrition Congenital defects of the germ plasm are often present despite a negative family history. Morbid heredity is much more evident in cases of progressive degeneration which begin in childhood, adolescence or even in adult life than those apparent at the time of birth or that appear during infancy.

The incidence of congenital anomalies, when calculated for the general population, is diluted to relatively insignificant figures there is one malformed child for every 200 infants born alive. The incidence of malformed infants born to parents who have had one malformed child is different According to Murphy and to Ballantyne, once a woman has given birth to a monster, for instance an anencephalic, subsequent children are more liable to show some form of monstrosity

Defects of Head and Nervous System at Birth. *Hydrocephalus.* Hydrocephalus is termed obstructive or communicative In obstructive hydrocephalus there are an immense variety of pathologic lesions productive of hydrocephalus all of which create an obstruction at some point in the pathway of the circulation of cerebrospinal fluid. The site of the obstruction may be difficult to identify

The terms communicating hydrocephalus, external hydrocephalus, and internal hydrocephalus have special meanings An external hydrocephalus is a condition in which excessive fluid accumulates in the subarachnoid space, whereas in internal hydrocephalus there is effusion of fluid within the ventricles

A *communicating hydrocephalus* arises when an excessive amount of cerebrospinal fluid is formed as the result of hyperemia of the choroid plexus with an ensuing excessive excretion or when there is a decreased amount of absorption of the normally formed fluid Common causes of this form of hydrocephalus are. infections and intracranial hypertension and occasionally increased intrathoracic pressure.

Hydrocephalus is often congenital in origin but it may be acquired, and often it is difficult to distinguish by clinical means the former from the latter.

In *congenital hydrocephalus* the developmental errors are usually situated at a point where there is normally a constricted passage for the flow of the cerebrospinal fluid, that is, at the foramen of Monro, the aqueduct of Sylvius, or the foramen of the fourth ventricle. The narrowed passage at one or more of these points is the result of a simple stenosis or an atresia Many of these developmental forms are truly internal hydrocephalus and affect the aqueduct of Sylvius "Forking" of the aqueduct is a common cause of congenital hydrocephalus, often associated with spina bifida, but compatible with long survival and minimal hydrocephalus should one of the channels be sufficiently well developed It has been clearly distinguished from so-called gliosis of the aqueduct, the essential pathologic changes of which are a proliferation of the subependymal glia and disruption of the ependyma

In the *Arnold-Chiari* malformations there is an elongation of the cerebellar tonsils, smallness and deformity of the medulla, smallness of the pons with degeneration of its transverse fibers and herniation of the cerebellum into the spinal cord Also a caudal displacement of the brain stem may cause this deformity

Many instances of the so-called idiopathic hydrocephalus are actually due to a low-grade meningitis, to thrombosis, or to hemorrhage which obstruct the flow of the cerebrospinal fluid

There are many infections which on healing may cause a hydrocephalus, for example, those due to the various pyogenic organisms, tuberculosis, syphilis, and toxoplasmosis. Extension of infection from the ear may cause a sinus thrombosis which is propagated into the tributaries or main venous sinuses and thus originates the so-called otitic hydrocephalus

Trauma and subdural hemorrhage are causes for hydrocephalus in some cases

Hydrocephalus causes a stretching and thinning of the cortex followed by atrophy and usually idiocy.

In congenital hydrocephalus, soon after birth the head begins to enlarge out of

proportion to the rest of the body. The fontanels bulge and later the lines of
of the skull separate. Vomiting and papilledema may be present in obstr
hydrocephalus.

On examination there are present all degrees of cranial enlargement. The
may be twice its normal size and actually weigh more than the body and ext
ties. Paralyses are rarely present. The cerebral ventricles are dilated and ther
atrophy of the brain and mental weakness.

The diagnosis is obvious in the well-developed instances of the disease.
differential diagnosis between the congenital and the acquired hydroceph
particularly that due to trauma and hemorrhage, may be made by aspiratio
the fluid and its replacement by air followed by roentgenologic examination

Ocular Hypertelorism (*Hereditary Craniofacial Dysostosis*). Ocular hype
rism is the result of an enlargement of the lesser wings of the sphenoid bone The
are set wide apart, the bridge of the nose is broad and, in some cases, flattened, the
diverge to an abnormal degree, frequently producing an external squint, exophtha
and optic atrophy The forehead is marked by a vertical groove extending upward
the root of the nose Mental deficiency of various degrees is usually associated How
when the deformity is mild, normal intelligence may prevail

Mild forms of this deformity are common and important because of the
pleasing appearance of the face

Platybasia. The essential feature of platybasia is the upward displacemen
the base of the posterior fossa formed by the basilar and condylar portions of
occipital bone This deformity in most instances represents a primary defec
development. However, it may result from rickets, osteomalacia and Paget's dise

In many instances there are no symptoms When symptoms are present,
are referable to the nervous system, and comprise weakness and spasticity of
extremities, from pressure on the pyramids. Clinical signs and symptoms cha
teristic of syringomyelia may occur in platybasia, and a syrinx in the cord may
present. Cerebellar ataxia, unsteadiness of gait and nystagmus are common S
nerve palsies and fifth nerve neuralgia may be present Papilledema and other s
of increased intracranial pressure may occur

The diagnosis depends on the demonstration by roentgenograms of the cha
teristic deformities of the skull

Congenital Defective Development of Integral Parts of the Nervous Syst
Defective development of integral parts of the nervous system occurs spontaneo
and may or may not be associated with birth injuries.

There may be defects in the development in the basal ganglia, or defects of
cerebellum may occur unilaterally and bilaterally and are associated with defic
development of the pons and olives.

The term nuclear aplasia is often applied to defects of the cranial nerve nuc
[illegible] amyotonia congenita

[illegible] by Josephy that if all ca
[illegible] of the brain, and som
times elsewhere, were collected in one group, there would exist a means of delimit
certain categories of disease For instance, many cases have been reported in wh
degeneration of the brain cells was associated with degeneration of the macula or w
retinitis pigmentosa, and in which degeneration of white matter was associated w
[illegible] From a consideration of these cases larger, rather fluid categories ha

names of one or more men who described them

The advantage of categoric arrangement is observed in Josephy's arrangement
the neuronal lipidoses. The changes characteristic of neuronal lipidoses include swelli
of ganglion cells, eccentricity of the nucleus, and replacement of peripheral Nissl bod
by prelipid granules

Essentially these changes are results of heredofamilial *disorder of lipid metabolis*

The neurologic manifestations cover a wide range, chiefly in the motor and intellectual spheres, and the retinal changes are those of a macular degeneration or atypical retinitis pigmentosa. Broadly speaking, the younger the patient, the more severe and of shorter duration is the disease, the older the patient, the less severe and of longer duration is the disease. The cherry red spot in the macula is more prominent in the former group of cases, the atypical retinitis pigmentosa, in the latter group

Some of the better known members of the group of diseases known as the neuronal lipidoses are: (1) Tay-Sachs (infantile type), (2) Spielmeyer-Vogt, (3) Batten-Mayou (juvenile type), (4) Kufs (late or adult type), (5) Refsum, (6) Niemann-Pick, (7) Hand-Schuller-Christian, (8) Gaucher, (9) Laurence-Moon-Biedl, (10) Pelizaeus-Merzbacher, (11) Krabbe (acute infantile), (12) Scholz (subacute juvenile), (13) Hallervorden-Spatz, (14) Greenfield and (15) Leber

Niemann-Pick, Hand-Schuller-Christian, Gaucher, Laurence-Moon-Biedl, and Pelizaeus-Merzbacher diseases are characterized by a lipoid reticuloendotheliosis and are described in this text with the diseases of metabolism (see Chapter 18)

Double hemiplegia is a bilateral paralysis with spasticity involving the arms more severely than the legs and often associated with pseudobulbar palsy and mental defect There is little tendency to improvement

The syndromes of *congenital athetosis, chorea,* and *rigidity* are attributed by Ford to defects of the basal ganglia

Double athetosis is recognized by the end of the first year when the child assumes strange postures and when the musculature becomes rigid when handled There is delay in holding up the head, sitting up and walking, and speech is delayed and imperfect In mild affections the child learns to walk and talk. During childhood there is an apparent improvement Before puberty improvement ceases and the condition remains stationary during the rest of life

The movements in *congenital chorea* resemble those of Sydenham's chorea, but the involuntary movements partake of the nature of athetosis, thus the term choreoathetosis Disturbances of speech, difficulty in swallowing, and facial grimaces may be prominent Mental development varies.

In *cerebellar ataxia,* when the child begins to walk, it falls frequently, and sways *from side to side as if sense of balance were defective. Strength may be good* and muscle tone may be normal or nearly so The difficulty in maintaining posture reveals an absence of postural tone The tendon reflexes are normal The rhythm of sp[illegible]

[illegible] If the symp[illegible] ife In many of the patients the disability is enhanced by the skeptical attitude taken by acquaintances Many of these patients improve year by year. In mild forms of the disease there may be almost complete recovery

Developmental Diseases of the Nervous System Manifested During Growth or During Adulthood. ***Friedreich's Ataxia.*** This is a heredofamilial disease of the nervous system which is transmitted by apparently normal as well as by affected individuals It is characterized by progressive degeneration of the spinocerebellar tracts, the corticospinal tracts and the posterior columns of the cord

The mode of transmission is obscure. The age of onset may vary within wide limits in different generations The disease occurs in both sexes

The first symptoms, occurring usually during childhood, are disturbances in gait consisting of a tendency to stagger and to fall The child is considered awkward Difficulties arise in learning to handle the utensils for eating, and in learning to write, and to speak distinctly

On examination it is observed that speech is often explosive and of irregular rhythm Articulation may be so defective as to be incomprehensible. There is a rhythmic nystagmus on lateral deviation, and the vision is impaired. A mild thoracic scoliosis of the spinal column is present. The feet have very high arches, pes cavus,

and hammer toe. The great toes are flexed at the distal joint and hyperextended the proximal joint Muscle tone is almost always reduced and postural tone especially affected The muscles may become wasted. In-co-ordination is prese All the tendon reflexes in the legs are lost early in the course of the disease. Th is cerebellar type of ataxia, more pronounced in the legs than in the arms. patient walks with a broad base. Oscillations of the head occur Station is unstea and swaying in the Romberg position is present.

The vibratory sense over the tibiae and the sense of position and of pass movements of the toes are lost or impaired. Two-point sense and stereognosis lost or diminished in the fingers

The patient becomes helpless and bedridden.

The presence of a positive family history, signs of cerebellar and tabetic ataxi disturbance in speech, nystagmus, positive Romberg's sign, loss of tendon reflex deformities of the feet and spinal column, terminal dementia, optic atrophy, bulb disturbances, and incontinence are diagnostic Second instances of the disease in family may be diagnosed on less evidence

In a few cases the disease seems to become arrested. The progress always so slow that death may occur from other causes before disability from the disea develops

Hereditary Spastic Paraplegia. Heredofamilial degenerative spastic par plegia is characterized by degeneration of the pyramidal tracts and clinically progressive spastic paraplegia

There may be a history that there was difficulty in learning to walk. There a tendency to walking on the toes and to pes equinus, equinovalgus or cavus, an claw toes are common Ankle clonus is easily elicited and the plantar response extensor. Later there is paraplegia-in-extension. This is followed by a position flexion at all joints of the legs and severe contractures The arms become spasti Dementia ensues.

Huntington's Chorea. Huntington's chorea is a chronic progressive chore associated with mental deterioration and inherited by both sexes as a dominan characteristic. There are sporadic instances of the disease which are clinically th same as the hereditary ones

This disease has been traced through many generations to its American origi in three brothers Both sexes are affected and either may transmit the disease

The symptoms, consisting of choreic movements, appear between the ages o 30 and 45 years, but a few patients have exhibited symptoms in childhood

On examination, in the beginning of the disease, the choreic movements ar abnormal only in their amplitude For instance, the normal movements of the face arms and hands appear at first as exaggerated gestures As the disease progresses the movements become rapid and violent and their amplitude is great In-co-ordination develops slowly until the patient is reduced to helplessness by it. Eventually the patient must be restrained to prevent injury, for the violent movements result in constant trauma Bulbar disorders such as loss of speech and inability to swallow ensue The mental disturbances include irritability, emotional instability and dementia

The diagnosis depends on the presence of chronic progressive chorea with dementia and often on the family history of similar sicknesses

The course of the disease is progressive and death results as a rule in from 10 to 15 years after the onset.

Developmental Disorders of Speech. The developmental disorders of speech are closely associated with the aphasias in adult life Orton attributed the following conditions to disturbances resulting from the failure to develop proper cerebral dominance which may be manifested by an uncertainty in the selection of a dominant hand; word deafness, word blindness, motor aphasia, agraphia, and

stuttering and stammering. These syndromes are found in pure or mixed form in all grades of severity.

Speech defects in the presence of normal hearing, intelligence, and the inability to understand speech when the speaker's lips are concealed, are idioglossia. Word deafness and idioglossia, without deafness, constitute an inability to understand spoken speech. Idioglossia affects boys more often than girls and occurs in all degrees of severity. The child develops a language of its own. The vowels are well formed and sometimes substituted for consonants, for only a few consonants are employed. The words are delivered very rapidly so that the effect is meaningless jabber even if sentences are properly formed. The prognosis is uncertain

Word blindness and mirror writing often affect several members of the same family, and members of several generations The child cannot learn to read and write, for it cannot distinguish between letters, such as *b* and *d*, *p* and *q* and *n* and *u*, and tends to read *saw* for *was*, *ton* for *not* and *form* for *from*. Spelling is grossly defective, especially spelling of written words

In writing with the right hand, *rat* becomes *tar* This writing from right to left is called mirror writing. When the left hand is used for writing, mirror writing is often performed consistently In these children there is a failure in development of proper ocular movements from left to right There is slow improvement

Stuttering. Stuttering may be defined as a disturbance in the rhythm of speech characterized by intermittent or irregular spasmodic blockage or repetition of sounds and words Stuttering, as it unfolds itself from its early onset, is an example of a disorder wherein the emotional factors gradually play a greater and greater part and, finally, assume a dominant role Boys are affected more frequently than girls

The cause for stuttering or stammering is unknown There are four theories of the origin of stuttering which are worthy of mention (1) A psychosomatic theory regards stuttering as due to a combination of organic and psychologic factors occurring at approximately the same time, the primary basic factor being a delay in myelinization of the cortical speech areas There is no anatomic proof for this theory. (2) Stuttering is an organic disorder of the language function According to this theory stuttering is considered mainly the result of a conflict between the two cerebral hemispheres caused by a lack of development of a dominant gradient, the disorder is related to left-handedness, in that normally left-handed children (see Handedness, p 221) who are forced to use the right hand may acquire a stutter because of a lack of development of a dominant hemisphere (3) Stuttering is a functional disorder, a psychoneurosis (4) Stuttering is a habit or a behavior that is learned (a "diagnosogenic" and a "semantogenic" disorder) According to this theory stuttering is due to a faulty diagnosis in a semantic environment This theory contrasts sharply with that of psychoneurotic origin. The psychoneurotic theory places the emphasis on the child whereas the diagnosogenic theory places the etiologic emphasis on the parents

The last three theories, like the first, are not supported by objective data.

At the onset the child of about 3 or 4 years may begin to repeat words or sounds There may be only an occasional slight hesitation in speech, and while speaking the child may stop suddenly as if groping for a word. In many cases a period of observation may be required before it can be decided definitely that the child stutters The normal or physiologic period of hesitancy or repetition of words is relatively longer in the child who is a stutterer than in a child who does not stutter Nonstutterers repeat words and phrases The stutterers' speech has a much greater proportion of syllabic repetition, owing to the spasmodic contractions of the muscles concerned with speech The spasm may be tonic, the parts involved remaining tense or showing only a slight quiver until the sound is forced through. In other cases the spasm is clonic, producing explosive repetition of the same sounds

As the stuttering becomes more definite, the parents become concerned, and

; told, "Speak clearly" or "Talk slowly. Think before you speak." The becomes conscious of his speech difficulty, and there is anxiety with nsions and spasmodic movements in other parts of the body such as of the eyes, jerking movements of the head, contortions of the face, of fists and stamping of feet may appear singly or in various combinang these spasms the stutterer frequently tries to speak on inspiration, t resulting in short inspiratory gasping movements until, apparently he forces out the word on expiration. Between the ages of 6 and 12 culties in personality adjustment may gradually develop. The child ensitive to ridicule and may resent correction The resultant loss of and security in speech situations may gradually lower self-esteem.

adolescent or the young adult stutterer, if stuttering is severe, there is ech with resultant difficulties in personality and adjustment. There is a shyness, and usually a sense of inferiority develops. Basically, however, lity of a stutterer as a whole is just as varied as that of the nonstutterer. capacity to lead a normal life by adjusting to the difficulty Usually lears in early adult life

ler adult stutterer is matured physically and emotionally. By trial and tern of speech has developed which has a minimum of stuttering Under otional excitement stuttering may occur, and despite normal intelligence st expert care the disorder may persist throughout life

gnosis of stuttering can be made only when the child stutters when he are no tests by which one can tell which child who begins unduly to to repeat words or sentences will start stuttering and which child will al speech Those who have stuttered during childhood have a great repeat words, phrases and conversation after they have ceased to

roclonus Multiplex (*Friedreich's Myoclonus*). This disease, which may occurs in middle-aged men more frequently than in women There are cklike contractions of the muscles of very brief duration. In the beginctions are fascicular but later the entire muscle or muscles are affected patient may fall to the ground As a rule there is a symmetric involve- proximal muscles of the arms and shoulders, but eventually all the scles are involved The diaphragm may show myoclonus There is no r atrophy The movements are increased by emotional excitement and luring sleep An attempt to elicit the tendon reflexes may induce violent . The violent contractions distort all volitional activity

re no demonstrable changes in the nervous system.

yelitis Optica. This disease occurs in both children and adults As a poradic condition, but McAlpine has described familial cases

verse myelitis and optic neuritis may appear simultaneously or sepa- of vision may appear without any prodromes One or both eyes may The ophthalmologist describes the appearances of the optic disks as pilledema. After a few weeks these changes begin to recede and they use pallor. The loss of vision develops rapidly. The central scotoma, absolute scotoma, enlarges, and in most cases the peripheral fields istricted. Within a few days after the onset the affected eye may be course of optic neuritis of this type is relatively brief, averaging perhaps ks to 2 or 3 months.

elitis may precede the optic neuritis, may occur simultaneously, or may months or years The onset is usually acute and may be attended with process is a disseminated one, but the clinical manifestations usually ransverse lesion of the spinal cord In most instances there is complete with anesthesia and loss of control of the bladder and rectum within the

course of a few days. Paraplegia-in-extension, paraplegia-in-flexion and flaccid paraplegia with loss of tendon reflexes may all occur. The process may become arrested at any stage, and there may be much more improvement than expected. Even complete paralysis may admit of a return of function.

If both optic neuritis and myelitis be present, and if other causes such as the encephalomyelitis of measles and vaccinia can be ruled out, the diagnosis of neuromyelitis optica seems to be justified.

The patient survives the first attack of myelitis and indeed often makes a complete or nearly complete recovery. Even severe optic neuritis admits of substantial recovery of vision. The ultimate prognosis, despite remissions of symptoms, seems to be unfavorable.

Hereditary Tremors. Hereditary tremors are common. They commence early in life and, once established, do not progress until middle life is attained, when progress may be resumed.

The tremor often occurs in members of successive generations. Both men and women may have this condition, and either may transmit it. The tremor affects the hands In some instances the head, tongue and legs may participate. The tremor begins during puberty, is accentuated by emotional reactions and fatigue, and is absent on relaxation The station, gait, and articulation are unaffected

There is never any improvement in the condition once the tremor has developed. If these patients are taught to adapt and adjust themselves, they may suffer minimal handicap from the presence of the tremor (see p 46)

CEREBRAL BIRTH INJURIES

The causes of cerebral birth injury in full term infants are maternal malformed and contracted pelves, often due to rickets, rigid soft parts, precipitate or prolonged labor, abnormal presentations, high forceps deliveries, breech extractions and overlarge fetal heads First babies are most frequently injured Owing to softness of the cranium, cerebral birth injury is perhaps more frequent in the premature babies than in mature infants The congenitally malformed nervous system is more susceptible to birth injuries than normally formed ones

Ford has expressed the belief that cerebral birth injury is the most frequent cause of *congenital hemiplegia* If syphilis, neoplasm and abscess can be etiologically eliminated, the history of birth will decide whether there has been a birth injury or whether there is some prenatal process The presence of convulsions signifies the degree of seriousness of the brain injury.

The mental condition resulting from cerebral birth injury comprises a mild or moderate deficiency in intelligence with little change in personality Some children and adult hemiplegics are so coddled and spoiled that they make a very bad impression, an impression which elaborates their mental deficiency rather than minimizes it.

A common birth injury is tearing of the small tentorial vessels. The blood then collects in a film on the upper surface of the cerebellum or on the upper tentorial surface Likewise injury to the cerebral sinuses and veins may be sustained

The monoplegias are often of crural and brachial distributions The crural monoplegias are more frequent than are brachial ones. In all of these the contralateral limb is often slightly involved Double hemiplegias resemble the congenital diplegias Athetoid movements of mild degree may be associated with either bilateral or unilateral paralysis.

Hemiplegia is the usual type of paralysis due to birth injury. There is underdevelopment of the affected arm, hand, leg and foot When there is considerable spasticity present, the affected hand is deformed to an extreme degree. Much less obvious is the deformity of a foot

Convulsive seizures occur in many of those who have a birth injury The convulsions may be confined to the affected members or may begin on the affected side

and become generalized. The focal attacks may be *jacksonian in type* l spread to involve the other cerebral hemisphere, in which case there is a consciousness. A severe focal convulsion is followed by increased weaknes affected limb which should clear up in a few days If the limb remains we *the presence of a brain tumor is suspected.*

The diagnosis depends chiefly on the history of birth. The chance of ir ment of manifestations, once expressed, is not good. The development of (makes the prognosis less favorable than it would be otherwise, since deter may be associated However, many of these deformed individuals reach (

BACTERIAL AND VIRAL INFECTIONS OF THE NERVOUS SYST

BACTERIAL INFECTIONS OF THE CENTRAL NERVOUS SYSTEM

Neisseria meningitidis (Meningococcus) and Epidemic Meningitis anc brospinal Fever. The *Neisseria meningitidis* is a gram-negative coccus, nc and nonspore-forming The meningococci are classified by bacteriologists in groups The organisms of these groups cause most cases of meningitis It appe: different epidemics may be caused by different types (I, II, III and IV) of mening but mainly by type I

A number of intermediate heterogeneous types of meningococci which are to each other and to the fixed types have been described The virulence of a pa type of meningococci cannot be determined, for these organisms do not dissoci: smooth (S) pathogenic forms and rough (R) nonpathogens

In about 7 of every 10 cases of acute meningitis the meningococcus etiologic agent Two patients in every 10 will have a pneumococcic mening the remaining cases the disease will be due to some other sort of germ or t infection.

Meningitis occurs most commonly in temperate climates during Nov December and January The infection is air borne Sporadic cases of meningo meningitis occur usually among children Negroes seem more susceptible those of other races Individual susceptibility is not predictable; often the and the robust are affected The disease is one that is easily spread when p are crowded close together in sleeping quarters For instance, epidemics are created in army barracks

Meningococcic meningitis seems to be transferred mainly by carriers, for (an epidemic there are many more carriers than there are persons who ha active disease The meningococcus is present in the nose and throat of many h persons The organisms may remain for a long time in the respiratory secreti those who have had the disease. There are three groups of carriers. (1) ch (2) intermittent and (3) transient

The meningococcus invades the body by first establishing a focus or loc infection in the respiratory passages A focus thus established may produce se *disease in the skin, joints, heart, eyes and ears* However, there is a tendenc the germs to be blood borne and to localize in the meninges of the central ne system

Meningococcic Septicemia. The cutaneous lesions of meningococcemi easily observed and accessible for examination (*Daniels*)

The cutaneous lesions of meningococcemia are the result of vascular in which consists of endothelial damage and inflammation of the vessels, often minating in thrombosis and necrosis The meningococci occur in these lesions when they are demonstrated, the specificity of the lesion is thus proved

The symptoms of a meningococcic septicemia are first those of disease of upper part of the respiratory tract After a period of from one to many days manifestations become more acute. There is a sudden chill with gradual or r

rise in temperature. Malaise, extreme weakness, aching of muscles, moderate headache, nausea, vomiting, pains in the joints or actual acute inflammation of joints develops

The cutaneous lesions of meningococcemia appear within 12 to 36 hours after the onset of the disease if they occur at all These lesions are macules, papules, nodules, vesicles, and petechial and purpuric lesions, they are situated over the lower extremities and the trunk. Papules often do not fade on pressure

Examination and observation will reveal that the temperature varies from normal to 105 F (about 40 5 C). The rash may be obvious or it may be so sparse that careful and frequently repeated search is necessary to find it.

A wide variety of forms of rash occurs. The commonest cutaneous lesion is petechial or purpuric eruption, the individual lesions vary from 1 to 15 mm. in diameter. In addition to this type of rash there are ill-defined, faintly pink macules similar to the rose spots of typhoid fever These may be evanescent, and occasionally a few of them may constitute the only cutaneous manifestation.

Maculopapular lesions are often present, and in a few there may be central petechiae. The larger ones are nodular or plaquelike and often tender. When on the extremities these resemble the smaller lesions of erythema nodosum. Petechiae occasionally are present in the conjunctivae and the oral mucous membranes. The macular lesions may recede with fall in temperature, only to reappear as the temperature again rises The rapidity with which the rash may appear makes it necessary to examine the patient at frequent intervals, for the rash may advance from a few indefinite spots to a widespread eruption in a few hours Large ecchymotic lesions may become vesicular and finally ulcerate

Herpes simplex is common, usually occurring about the second day of the illness Herpes zoster involving the ophthalmic and maxillary branches of the fifth cranial nerve has been recorded

It is desirable to diagnose meningococcic septicemia before meningitis develops, for a meningitis may be prevented by appropriate chemotherapy or antibiotic therapy.

The diagnostic value of smears from the purpuric lesions of the skin in meningococcic disease is illustrated by the work of Tompkins, who found positive cutaneous smears in 39 of 48 cases Positive smears may be obtained when blood cultures are negative

Meningococcic Meningitis (Epidemic Meningitis, Cerebrospinal Fever, Spotted Fever) The prodromal period and the meningococcic septicemia have been described.

SYMPTOMS After the prodromal period the onset of the disease is usually acute There are different symptomatic types of the disease· (1) fulminating, (2) the acute common type, (3) subacute or chronic and (4) the abortive

The fulminating type of the disease frequently occurs at the beginning of severe epidemics The symptoms commence with an intense headache, chills and high fever. In some instances the victim falls suddenly without warning as if stricken with apoplexy There is prostration with pallor and cyanosis and coma In those in whom the infection is overwhelming, the temperature may be normal or subnormal. There are petechiae and large purpuric spots in the skin (see Meningococcic Septicemia, p 1140)

The common signs of meningeal irritation are often absent. Hemiplegia and other evidences of focal cerebral lesions may develop as a result of purpuric lesions in the brain An extremely fulminating type of this disease termed the *Waterhouse-Friderichsen syndrome* is associated with hemorrhages into the adrenal glands and diffuse widespread hemorrhages into the skin The pulse is irregular, rapid and

feeble. Respiration is rapid and irregular. The spinal fluid is clear at first but soon there is an excess of leukocytes. The *meningococci are recovered in cultures and* often are found in smears. The entire course averages between 1 and 2 days.

The *acute common type* of meningococcic meningitis is symptomatically characterized by malaise, catarrhal rhinitis, sore throat and cough lasting for a few days to 2 weeks The temperature then rises to 104 F (40 C) within a few hours One or more chills and headache occur. Hyperesthesia, rigidity of the spinal column and often opisthotonos develop. There may be delirium and stupor. The pulse is rapid (120 to 150) and may be irregular. Respiration may be either rapid or slow. Petechiae are common but purpura is unusual

On examination the findings are the same as in the fulminating type of the disease but less severe.

In the most favorable *instances the disease runs a course of from 1 to 2 weeks.* With or without treatment, in a few cases toward the end of the first week the temperature begins to fall, the mental condition improves and the spinal fluid clears Usually the temperature falls by lysis but in some cases termination by crisis has been observed Cervical rigidity usually diminishes as the other symptoms do, but occasionally may persist after the spinal fluid and the temperature become normal.

In the unfavorable instances death is preceded by deepening coma, relaxation of the musculature and hyperpyrexia. Throughout the course meningococci are found in the spinal fluid.

Meningococcic meningitis does not often persist more than 2 weeks When of longer duration, the disease becomes *subacute or chronic.* In such instances the *temperature slowly diminishes until fever is irregular and the meningeal irritation* continues. The patient may recover, but more frequently hydrocephalus ensues which often is fatal In some cases the course of the illness is characterized by remissions and exacerbations.

The chronic type of meningococcic meningitis is observed after epidemics The onset commences with vague symptoms such as fever, anorexia and vomiting The general symptoms are those of an infection The symptoms attributable to the nervous system are those due to an increased intracranial pressure.

Vomiting, headache and deterioration of cerebral function and vision result from intracranial hypertension. Diarrhea and incontinence are frequent and severe in those seriously ill from meningitis

The *abortive type* of meningococcic meningitis is manifested by malaise, headache and perhaps pain in the back There may be fever and a mild chill. Meningococci are found in the nasopharynx but the symptoms disappear within a few hours and no signs of meningeal irritation ever develop

Worster-Drought and Kennedy distinguish between those cases in which the symptoms disappear spontaneously, the true abortive type, and those in which the favorable course is the result of prompt treatment

Examination The nervous system may be destitute of positive findings In some, very soon after the onset, *there is pain in the back and legs. In children,* convulsions may be observed. Very soon the muscles of the neck and back become painful and stiff, with cervical retraction or even opisthotonos There are photophobia, hyperacusis, delirium, followed in severe disease by stupor or coma. Strabismus is frequent. Nystagmus, ptosis, irregularity of the pupils, and facial spasm may be present. Impairment of sight or hearing may be found There are often general cutaneous hyperesthesia, and tenderness along the spinal column, with tremor, and occasional tonic or clonic spasms of the extremities The joints may be red and swollen. Kernig's sign is usually present The spleen may be palpable.

Breathing is rapid, shallow and irregular Pallor and cyanosis may be present from the onset The pulse is rapid and often irregular except in those in whom

increased intracranial pressure causes bradycardia Blood pressure is low. The temperature varies, but may be subnormal until death ensues as the result of a fulminating infection. In all there is fever at some period during the active stage of the disease. The temperature ranges between 100 F (37.8 C) and 105 F (about 40.5 C).

The cutaneous manifestations, as described under meningococcic septicemia, are erythema, labial herpes, petechial hemorrhages and large purpuric lesions

The blood shows a constant leukocytosis, the count averaging between 15,000 and 30,000 per cubic millimeter The polymorphonuclear leukocytes average between 80 and 85 per cent of the white count but may be greater In rare cases leukopenia may prevail. Often results of blood culture are positive on the first day of the illness.

The spinal fluid may be normal on the first day In some there is only a slight increase of cells. In almost all, however, there is a great increase in the cell count which ranges from a few hundred to many thousands. The fluid may be opalescent, cloudy, turgid or purulent, depending on the number of cells it contains Polymorphonuclear leukocytes usually predominate but the lymphocytes also are increased. In those in whom convalescence is slow the lymphocytes become relatively more numerous. The spinal fluid is under increased pressure which may not be evident due to an increased viscosity The globulin is increased The total protein concentrations may reach 500 mg per ml. The fibrin is often increased and a film may form on standing Sugar and chlorides are diminished. Sometimes a spontaneous coagulation of the spinal fluid may have resulted from its increased protein content and obstruction of the spinal canal The meningococci often are difficult to demonstrate in smears of the spinal fluid

Diagnosis The diagnosis of meningococcic meningitis depends on the demonstration of the organism in spinal fluid or in a cutaneous lesion or the joint effusion, or in the blood provided the essential manifestations are present in association with the foregoing findings

The prognosis depends on the virulence of the invading organisms, host resistance and the promptness with which treatment is instituted The presence of hydrocephalus with thick or coagulated spinal fluid (Froin's syndrome) renders the chances for recovery very bad Under unfavorable conditions half of those who have the disease may succumb

Pneumococcic Meningitis. A pneumococcic meningitis may be suspected by the development of signs of meningitis during the course of pneumonia, but is established only by the demonstration of the organisms in the spinal fluid where they are usually abundant The fluid may be clear for a time when the meningitis is circumscribed Signs of meningeal irritation without any change in the spinal fluid may occur at the onset of pneumonia as in any other severe acute infection These are attributed to intoxication rather than to bacterial invasion of the meninges, and the term meningism is often employed to designate this syndrome

The examination of the spinal fluid reveals the presence of pneumococci. This is the only certain diagnostic criterion

The mortality rate was extremely high until the introduction of the sulfonamide series of drugs in therapy.

Meningitis Due to Staphylococci and Streptococci. The pathogenic staphylococci and streptococci cause severe meningitis *Staphylococcus aureus* (*Micrococcus pyogenes* var *aureus*) and *Streptococcus hemolyticus* are the commonest

The diagnosis depends on the presence of the symptoms and findings of meningitis and the identification of the organism in the spinal fluid.

Prognosis has improved since modern antibiotics have been used in therapy of these diseases In the past a few patients survived but this was exceptional The

number of colonies of staphylococci and streptococci grown on culture of the spinal fluid is of some prognostic importance.

"Influenzal" Meningitis. The causative organism, termed Pfeiffer's bacillus or *Bacillus influenzae (Hemophilus influenzae)*, may cause severe meningitis.

The diagnosis depends on the study of the spinal fluid The high cell count establishes the presence of meningitis and the recovery of the organism reveals the nature of the infection

Otitic Meningitis. *Otitic meningitis is due to the entrance into the space within* the subarachnoid by such bacteria as the streptococcus, the pneumococcus or the staphylococcus The infection originates from foci about the middle ear or mastoid cells. The extension of the purulent labyrinthitis occurs through the internal auditory meatus or by necrosis of the bony capsule, by rupture of a petrous apical abscess, by the spread of infection from the lateral sinus thrombosis, by rupture of a brain abscess into the ventricle or the subarachnoid space, or by the accidental opening of the dura during an operative procedure about the mastoid petrosa.

The symptoms and signs of otitic meningitis begin with generalized headache of increasing intensity, a chill and sustained high fever, vomiting, drowsiness, irritability, hyperesthesia of the skin and muscles, changes in mentality, stupor and convulsions

There are stiffness of the neck, a positive reaction to Kernig's turning test, irregular nystagmus, muscle twitching, hyperemia, papilledema of the optic nerve head and paralysis of the cranial nerves, especially the abducens. Later there are widespread flaccid paralysis, incontinence, fast pulse, dilated pupils without reflexes, deep coma and death (see p 99)

The diagnosis is established by examination of the spinal fluid In the purulent form of the disease the fluid contains increased leukocytes, an increased amount of globulin, decreased or absent sugar and decreased chloride

Otitic hydrocephalus is characterized by papilledema, lateral paralysis of the abducens, and the fact that the normal spinal fluid is under extremely high pressure, there are few other symptoms. In this condition recovery usually follows repeated spinal drainage In otitic meningitis the prognosis depends on effective use of chemotherapy

Otitic, suppurative and serous forms of meningitis may resemble tuberculous, meningococcic, influenzal and syphilitic forms of the disease. The differential diagnosis is made from the clinical history, serologic reactions and the results of smears and cultures of the spinal fluid.

Nonsuppurative Encephalitis of Otitic Origin. There is a condition of inflammation or encephalitis which may not be too serious when infection enters the brain from an adjacent focus in the skull It usually occurs in the temporal lobe from mastoiditis or its complications. In this form of encephalitis, which is subacute and localized, there are focal signs of the lesion in the brain adjacent to the suppurative focus in the skull. These signs are changeable, varying with the amount of edema in the portion of the brain surrounding the focus The signs greatly resemble those produced by infection of a temporal sphenoidal lobe or by a cerebellar abscess.

Lateral Sinus Thrombosis. A lateral sinus thrombosis does not always produce symptoms. A nonobstructive and aseptic thrombus is without symptoms other than those of the middle ear disease. When symptoms are present, they are those of infection. There are *chills in the afternoon followed by fever up to 104 F (40 C)* or higher, accompanied by severe headache and vomiting Often the chill is of short duration and is followed by sweating and a rapid descent of the temperature to normal or almost to normal Soon metastatic abscesses in the bones, joints, and lungs or other internal organs appear and portend the seriousness of the illness

In some instances of lateral sinus thrombosis the thrombus descends the internal

jugular vein, producing tender swollen regions around its course in the neck, and may penetrate into the superior petrosal sinus and the cavernous sinus These secondary intracranial complications may terminate the patient's life.

Ophthalmoscopic examination may reveal papilledema if a brain abscess is present The papilledema may be greater on one side than the other, and at times may reach 5 or 6 diopters In the beginning the papilledema may be observed in a patient having at the time minimal clinical symptoms

Tuberculosis of the Nervous System. The following forms of tuberculosis of the nervous system are described (1) tuberculous meningitis, (2) tuberculoma of the brain and spinal cord, (3) tuberculous spondylitis with involvement of the spinal cord, (4) tuberculosis of the bones of the cranium and (5) neuritis associated with tuberculous infection

Here only *tuberculous meningitis* and *tuberculomas* (see Abscess of the Brain, p. 1146) are considered Tuberculous spondylitis and tuberculosis of the bones of the head have been described with diseases of the bones Neuritis associated with tuberculous infections is the sort described under interstitial neuritis

Tuberculous Meningitis. Tuberculous meningitis is almost always due to the human type of organism The disease is most frequent during the second year of life although it may develop at any age It usually occurs during the winter or early spring and frequently follows measles, pertussis or other acute infectious disease.

Tuberculous meningitis may be a part of a generalized meningo-encephalitis or of a generalized meningitis associated with solitary tubercle A localized meningitis, subacute or chronic, may be present occasionally

In the beginning there are lack of energy, anorexia and loss of body weight, headache and vomiting The temperature may reach 101 F (38 3 C) and the pulse is rapid Episodes of irritability and excitability may alternate with apathy, drowsiness and stupor. In some instances the stupor clears and symptomatic improvement follows and lasts for a week or two, at the end of this period the patient sinks into a deep stupor and finally into coma The fever returns and the temperature rises to 105 or 106 F (40 5 or 41 C), the pulse is slow and irregular and the respiration is periodic.

Sixth nerve palsies, localized muscular twitchings and various automatic movements as well as focal and general convulsive seizures are often observed Often early, and always in the late stages, congestion of the retinal veins develops and there is papilledema which may reach a height of several diopters.

There are irregularity and slowing of the pulse. The heart action becomes progressively weaker and with this the pulse rate increases In the early stages of the disease there are narrowing of the pupils and photophobia As the intracranial pressure increases, the pupils dilate and become irregular and there may be conjugate deviation There may be involvement of the third nerve on one side and paralysis of the face, limbs and hypoglossal nerve on the opposite side (Weber's syndrome) Tubercles in the choroid are common.

Tremors, athetoid movements, paralysis and hemiplegia may be present. Facial monoplegias are common, other monoplegias may be present Kernig's sign and plantar extension are sometimes present

The cerebrospinal fluid is but slightly changed in the early stages of the disease. The pressure becomes increased and the fluid is clear or at most slightly opalescent The cell count, chiefly lymphocytic, is relatively low at first but slowly rises to 100 or 200 or more per cubic millimeter. The globulin and total protein are greatly increased Sugar estimations may give results within normal limits at the onset but the values decrease When the fluid is permitted to stand a while, a delicate fibrin film usually forms and this contains tubercle bacilli Inoculation of a guinea pig usually will give positive evidence of the presence of tubercle bacilli.

There is no leukocytosis in the early stages of the infection, but toward the end

the leukocytes may number 30,000 per cubic millimeter of blood Reaction intracutaneous tuberculin test is almost always strongly positive at the onse during the early stages of the illness, but toward the end it may become neg

The diagnosis is based on the presence of the clinical findings as describe the presence of tubercle bacilli in the cerebrospinal fluid. Reaction to the tube skin test, the physical signs of tuberculous disease in the thorax, bones or l nodes, and the history of exposure to infections are diagnostically helpful

When the diagnosis is fully proved, a fatal outcome is expected The diag is fully proved by cultures or obtaining the organisms by guinea pig inocu from the spinal fluid

Subdural Abscess of the Cranium. Subdural abscess of the cranium r from otitis and mastoiditis or from nasal sinusitis. The onset of symptoms is us preceded by evidences of otitis or of nasal sinus infection. There are heada fever, stiff neck, drowsiness, stupor, focal convulsions on the contralateral side aphasia followed by hemiplegia This disease usually runs a rapid course to e death of the patient

A correct diagnosis cannot be made until the skull is trephined and the t studied histologically and tubercle bacilli demonstrated.

Abscess of the Brain. The common causes of acute bacterial meningitis w arise in association with middle ear and mastoid infections are discussed in cor tion with diseases of the middle ear (Chapter 4) It is obvious that some of t infections may reach the brain and originate an abscess therein

Here we shall discuss mainly those brain abscesses which arise *in associa* with chronic otitis media, infection of the nasal sinuses, subacute bacterer septicemias, and abscess which may follow a relatively mild infectious diseas one associated with a staphylococcic infection and osteomyelitis. The streptoc pneumococci, *Escherichia coli* and anaerobic organisms may cause brain absce Staphylococci, streptococci and *Escherichia coli* may be the casuative organism brain abscesses after trauma to the skull

In these less acute abscesses the infection reaches the brain through the bl stream If the symptoms of a blood infection are slight, it is difficult to contemp the nature of the expanding brain lesion

If there should be a history of syphilis and if there is a positive serologic r tion in the blood or cerebrospinal fluid, a *gumma* may be suspected, and the pat should be given the benefit of energetic antisyphilitic treatment for a time If th is a highly malignant glioma present, nothing will be lost by postponement surgical intervention Gummas may resist treatment, and it may be necessary remove a cerebral syphiloma by operation

Tuberculous disease of the basal cranial bones may extend to the meninges brain within, largely by setting up thrombophlebitis in one or other of the g venous sinuses. Thus the cavernous sinus may become thrombosed in *tubercul* of the anterior fossa, while the lateral sinus may become implicated *in disease* the middle or posterior fossa

Tuberculomas of the nervous system are the result of blood-stream invasion the tubercle bacilli. The invasion of the brain by this method is relatively *rare*, si tubercles which simulate neoplasm of the brain comprise a very small percent of all intracranial tumors

In tuberculoma the temperature is often subnormal and irregular, with oc sional rises to 100 F (37.8 C) The blood shows a polymorphonuclear *leukocyto* Finally the abscess bursts, producing a fulminating purulent ventriculitis or me ingitis; the pulse and temperature increase and the patient dies, and then the corr diagnosis is made Or the abscess may evacuate itself spontaneously, usually inco pletely, into the middle ear or accessory air sinus from which the infecti

originated. If there has been an opportunity for parasitic infection, such infection may localize in the brain and cause an expanding lesion, a parasitic cyst.

Tuberculoma is often manifested by signs of focal cortical irritation such as jacksonian fits, but not by paralysis or other physical signs. Increased intracranial pressure develops late and the disease runs a very slow course, sometimes lasting for several years.

The diagnosis of many tuberculomas is made at the time of operation for suspected neoplasm of the brain The presence of signs of multiple lesions or of lesions in the cerebellum or brain stem favors the diagnosis of tuberculomas if Recklinghausen's disease is not present In almost all instances in which the diagnosis is established, death ensues.

Parasitic cysts of the brain comprise two chief varieties, (1) hydatid cyst and (2) *Cysticercus cellulosae*

The hydatid cyst represents the cystic stage in the life history following the ingestion of the ova of *Taenia echinococcus* (see p 939)

Hydatid disease may be suspected as the cause of an expanding tumor of the brain in natives of Iceland, Greece, and Australia The hydatid cyst may be single or multiple. When solitary, it may attain a large size

The complement fixation test on the blood serum with a suitable antigen, the cutaneous reaction to an intradermic inoculation of sterile hydatid fluid, and the presence of eosinophilia of the blood and the cerebrospinal fluid are helpful diagnostically when these cysts of the brain are suspected

Infection with *Cysticercus cellulosae* follows the ingestion of the ova of *Taenia solium*. Multiple cysticercal worms develop and become encysted in the muscles and subcutaneous tissues and in the brain and its meninges or in the vitreous humor of the eye. When in the course of time these cysts undergo calcification, they become visible roentgenographically. In the muscles and brain the roentgenographic shadows are pathognomonic

The symptoms of cerebral cysticercosis depend on the situation of the encysted parasite A convulsive disorder is the common manifestation Eosinophilia of the blood and the cerebrospinal fluid sometimes will be helpful in the initiation of a proper investigation

A brain abscess forms in much the same way as an abscess elsewhere There is first the diffuse localized stage of engorgement, or localized acute encephalitis, in which there appear regions of softening and liquefaction These regions enlarge, coalesce, lose their red color and form pus The surrounding brain tissue reacts by forming about the abscess a definite limiting wall which is composed of a dense fibrous tissue surrounded by a zone of gliosis

SYMPTOMS. If the abscess is originated by a virulent infection, as has been described in diseases of the ear, it may extend rapidly, the fever remains high, the leukocytosis continues and headache, vomiting, drowsiness and finally stupor ensue Death may occur within 2 or 3 weeks

In less virulent infections the course is different Fever, leukocytosis and other signs of infection disappear The temperature often is subnormal If the abscess does not occlude the ventricular system or give rise to focal signs, the patient may appear well The process may stop, but usually increasing pressure within the abscess causes rupture of the inflammatory tissue which confines the abscess, with extension of the infection to the surrounding tissues This is made evident by a recurrence of the fever and by focal signs A meningeal reaction may occur and subside, or a purulent meningitis may ensue. The infection may again become walled off by an inflammatory reaction, and the signs of infection may again disappear Such remissions and exacerbations of symptoms are frequent Eventually death occurs from increased intracranial pressure, extension of the infection into the ventricles or the meninges or throughout the brain. Symptoms from an abscess

which follows a compound fracture of the skull may not occur for months, or years, after the head injury The patient appears healthy; this may be the c in injuries of the brain received in various accidents.

Frontal abscess commonly arises as a result of direct infection from the fro ethmoidal, or sphenoidal air sinuses The significant findings are mental dull deficient control of sphincters, loss of the abdominal reflex on the side opposi the abscess, and the presence of an extensor plantar reflex on this same side. triculograms are often useful in demonstrating deformity or displacement of adjacent lateral ventricle

A *temporal abscess* is easier to recognize when situated superficially in the temporal lobe in right-handed persons, for in right-handed persons lesions of left temporal cortex produce impairment of the auditory memories of spoken wo Hence in a left-sided temporal abscess the patient tends to have dysphasia makes mistakes in naming objects Large frontal abscesses situated in either may press inward toward the corona radiata and cause a facial or faciobrac monoplegia As the result of pressure backward toward the angular gyrus, h anopsia may ensue. Even when the abscess is far forward, it may press on fibers of the optic radiation, causing a visual field defect. Visual defects of this are difficult to verify, owing to the patient's mental dullness Extension downw toward the floor of the skull and the ocular nerves may cause dilatation of pupil, ptosis and impairment of external ocular movements on the side of the absc

A *cerebellar abscess* causes vertigo, hemiataxia and hypotonia of the limbs the side of the abscess, with spontaneous mispointing on Bárány's pointing t conjugate deviation of the eyes to the side away from the abscess, and nystagn A cerebellar abscess may induce acute ventricular hypertension with a rapid incre in pressure causing sudden respiratory paralysis and death unless the abscess be localized and promptly evacuated

Multiple abscesses originate from metastatic blood-borne infections and may situated anywhere in the brain, but are common in the parietal and occipital lo

In *multiple cerebral abscesses* the focal signs depend on their situations. C monly one abscess produces the symptoms, while evidences of the other coexist ones are absent Mental confusion and headache are the common symptoms. M tiple abscesses may cause several widely scattered focal lesions which indic multiple lesions.

Chronic *localized serous arachnoiditis* or *meningitis serosa circumscripta* chronic arachnoiditis) is generally a sequela of chronic otitis media and usuall is situated in one or other pontocerebellar recess This process is often the ca of the condition known as *pseudotumor cerebelli* It consists in a local accumulat of cerebrospinal fluid in a thickened and obstructed lateral cistern, causing obstructive hydrocephalus which often produces intracranial hypertension There usually a permanent unilateral impairment of hearing The impaired hearing a intracranial hypertension are characteristic too of an acoustic neuroma from wh differentiation is made only by an exploratory operation

Pseudotumor cerebri is a term applied to the condition in which the clini signs of brain tumor appear, followed by complete recovery, or in which ventricul grams or necropsy do not reveal a lesion which can account for the symptoms

There are instances of pseudotumor cerebri in which the symptoms arise fro an acute otitic hydrocephalus or serous meningitis of the ventricles which is reliev by puncture of the ventricle.

EXAMINATION. Abscesses of the frontal lobes may give minimal signs of loca zation. When the abscess is on the left, aphasia is common There is a loss mental alertness which may be accompanied by stupid jocularity and motor apath

When the temporal lobe is the site of abscess, homonymous defects in t ... Focal paresis is sometimes present. Alterations

the tendon reflexes with the plantar extensor are often present on the side opposite to the abscess.

Abscess in the cerebellum produces in-co-ordinate equilibratory muscular activity. There may be muscular hypertonus and cerebellar fits; more often, there is a disturbance of postural fixation with atonia of muscles. Nystagmus is horizontal and is most evident when the eyes are deviated toward the side of the lesion Suboccipital tenderness and headache are common symptoms of cerebellar abscesses.

The spinal fluid reveals 20 to 100 cells, chiefly lymphocytes, per cubic millimeter. There are normal sugar and chloride content and elevation of the proteins to between 50 and 150 mg. If the abscess leaks from time to time, there is a preponderance of leukocytes. If the cell count is not high and bacteria cannot be cultivated and if the sugar and chlorides are not diminished, the condition is a meningeal reaction which will subside. Decrease of the concentration of the chlorides and sugar and rapid rise of the polymorphonuclear leukocyte count indicate an impending purulent meningitis.

DIAGNOSIS. The diagnosis of brain abscess usually can be safely made if there are symptoms of a general infection and evidences of an increased intracranial pressure There should be signs of a focal cerebral lesion, the history of some preceding infections such as otitis media or of trauma, and the presence in the spinal fluid of from 20 to 100 cells, chiefly lymphocytes, per cubic millimeter. The diagnosis may be difficult and may require a period of observation or ventriculograms and surgical exploration

THE VIRAL ENCEPHALITIDES

The term neurotropic agent implies the affinity of any disease agent, irrespective of its nature, for the nervous system

The terms encephalitis, encephalomyelitis, polioencephalitis, poliomyelitis and leuko-encephalitis when employed in a general way imply infections of regions or particular tissues of the nervous system. These terms, while not confined to viral infections, are commonly employed thus and some of them are employed almost entirely to designate viral infections, for instance, poliomyelitis usually refers to poliomyelitis of viral origin

A number of endemic and epidemic infectious diseases of the central nervous system are produced by neurotropic viruses, for instance (1) type A, Vienna type, von Economo's or European encephalitis, (2) type B, which includes Japanese B encephalitis, Saint Louis encephalitis, equine encephalitis, (a) western, (b) eastern, and (c) Venezuelan, and Australian X disease, (3) Russian tick-borne encephalitis, (4) poliomyelitis and (5) rabies Poliomyelitis was described in Chapter 6

Infections of the nervous system by filtrable viruses affect chiefly the gray matter of the neuraxis These infections have a selective tendency to certain structures, for instance, epidemic encephalitis injures the substantia nigra, rabies, the bulbar nuclei, and poliomyelitis, the anterior spinal gray matter All may occur in either sporadic or epidemic forms, and there is usually a definite seasonal incidence and a tendency to select individuals of the same age group Epidemic encephalitis is unique in that it is characterized by a chronic phase, known as Parkinson's syndrome, which follows the acute phase after a prolonged remission

Epidemic Encephalitis (Encephalitis Lethargica) This disease is known also as the Vienna type of encephalitis, von Economo's disease, type A encephalitis, epidemic encephalitis, and sleepy or sleeping sickness The disease is a meningoencephalomyelitis The consensus is that the disease is a viral infection, and the virus has been termed virus A.

The brain in the acute phase of the disease is diffusely congested and contains small hemorrhages which are more intense in the basal ganglia and brain stem than in parts of the brain There may be scattered areas of meningitis.

Epidemic encephalitis appears in the winter months It is not trans person to person, for it is unusual for more than one member of a hous affected. The incubation period is not established. No age is exempt, highest incidence of encephalitis is in the second and third decades. You and even infants may be affected. The disease may attain pandemic pro it did in 1918 However, sporadic instances of the disease are common.

On the basis of symptoms three stages of the disease are describe acute stage, after which all symptoms disappear or there is progression the chronic stage, (2) the stage of remission, which may last for years d the patient seems well, and (3) the chronic stage of the disease which is first recognizable manifestation of the disorder Rarely can the first stag nized, and then in retrospect when the third stage is evident The seco the disease is not manifested and therefore not recognizable

Acute Stage of Epidemic Encephalitis The acute form of the disease is as an acute infection of the upper part of the respiratory tract In retrospe may be obtained which implies that during the supposedly respiratory inf were pains of a radicular distribution, myoclonic twitchings, and diplopia however, some patients who have a severe acute onset of symptoms definite, and these definite types are designated as the somnolent-ophth type, the hyperkinetic type, early development of symptoms of the pa syndrome, and the fulminating type

In the somnolent-ophthalmoplegic type of encephalitis the patient li deep sleep The patient may be aroused easily and will then respond but immediately relapses into somnolence, which may deepen to stupor a coma When the patient is aroused, radicular pains, local hyperesthesias a gias may be complained of If fever is present, the temperature is not 103 F (39 4 C)

In the hyperkinetic type of encephalitis the disease is more severe t somnolent-ophthalmoplegic type The onset is abrupt, fever is high There ment, restlessness and insomnia, confusion or disorientation, anxiety, ap and hallucinations. There may be sharp severe pains and myoclonic twitch extremities

Involuntary choreiform movements may be observed which may be a oculomotor palsies The pupils are unequal, and myosis and loss of the ligh frequent The course is often brief, and if the patient survives, the overac for several weeks The mortality rate is high

In the acute parkinsonian syndrome type of encephalitis the patient conscious without expression, change of position or movement for ma When movements are made they are slow and weak, and there may be a tremor initiated by movement The temperature often is normal. These pa begin the manifestations of the chronic parkinsonian syndrome while acute the disease

In the fulminating types of the disease a bulbar palsy develops rapidly cause of death Fever may be absent; if fever is present and of intermittent temperature rarely rises above 103 F (39 4 C) Hyperpyrexia is presen who do not survive the illness

Bulbar palsy is identified by difficulty in swallowing, and weakness o palate and the tongue with occasional fibrillary twitching

A reversal of the hours of sleep may occur in acute encephalitis. I common in chronic encephalitis. Often most of the daylight hours are sleep, but as night approaches the patient becomes active and restless. A the reversal of sleep is a transient phenomenon.

jerks affect the abdominal musculature, the face, shoulders, arms, legs and muscles of respiration Hiccough is common.

Bilateral extra-ocular palsies are incomplete, complete or transient Ptosis of the lids is common, The pupils may be dilated and inactive to light and during accommodation Nystagmus is often present.

Facial palsies are usually incomplete and transient Trismus is mild Paralysis of the extremities, hemiparesis and monoplegias are sometimes present. The tendon reflexes are normal.

The urine may contain albumin and occasionally and transiently sugar The leukocytes range from 15,000 to 30,000 per cubic millimeter with a slight increase in the polymorphonuclear leukocytes. The spinal fluid is normal in the early stages except for a moderate increase in lymphocytes ranging from 20 to 100 and rarely exceeding 200 per cubic millimeter

Chronic Stage of Epidemic Encephalitis (Parkinson's Syndrome) A chronic stage of encephalitis is peculiar to the virus A type of infections Rarely is there a history of an illness which can be said to be the acute phase of the disease and which definitely dates the beginning of the illness. The symptoms of the chronic stage of epidemic encephalitis advance slowly and uniformly without fever or other signs of infection

The *pathologic changes* present in the gray matter of the mesencephalon and diencephalon are degenerative, inflammatory, infiltrative and perivascular

In this syndrome the outstanding *manifestations* are those of extrapyramidal neuron lesions (see Organization of the Motor System, Chapter 6).

The parkinsonian syndrome is characterized by an altered posture with flexion of the trunk and extremities, by hypertonicity of the muscles characterized by a cogwheel phenomenon on extension of the muscles and by slowness of all movements, by expressionless face, rhythmic tremor during rest, and absence of associated movements when walking Repetitive movements are frequent and may persist for years.

The head may be tilted and rotated as in spasmodic torticollis The spinal column may be twisted and curved and the hips and shoulders held in asymmetric postures.

The lack of expression is sometimes replaced by a rigid smile, the jaws are often widely opened, the tongue is protruded and the head retracted The rigidity may become so severe eventually that the patient is virtually paralyzed

There are slow movements of large amplitude which occur at regular intervals (bradykinesia).

Tremors may involve the lips, face, eyelids, jaws and other parts of the body but are commonest in the hands and head In many patients these spasms disappear when the patient relaxes Intention tremors are rare in encephalitis

An *oculogyric crisis* is characterized by a sudden fixed stare followed by the eyes being rolled upward or to one side and fixed in that position The eyes cannot be returned to a normal position during the attack although they may be moved about in the main fixed position The attack is accompanied by severe pain in the eyeballs. Grimaces and rotation of the head and distortion of the trunk may be performed during the attack. Hallucinations, catatonic or trancelike states or anxiety may transpire during the fit The duration of the crisis varies from minutes to hours.

There may be disturbances in respiration characterized by increase in the respiratory excursion until after a few minutes respiration becomes violent. The mouth is widely opened, and the patient is frightened. After minutes or a few hours the disturbance slowly subsides The excessive ventilation may lead to tetany and prolonged

turbed

holding

Ble

When the lids are closed tightly, they cannot be opened by the patient for several seconds, but once they are opened, either by a violent effort or by the fingers, the spasm disappears *Myotonus of the lids* may be present.

Excessive salivation is common Hyperhidrosis, localized edemas, cyanosis and various disturbances of vasomotor innervation occur

The psychic changes in adults are trivial In children the natural inhibitions and fear of consequence may be lacking. Such children may steal, lie, destroy property, commit various offenses, run away from home, and physically mutilate themselves

DIAGNOSIS OF EPIDEMIC ENCEPHALITIS In the acute stage, encephalitis, tuberculous meningitis, lead encephalopathy, encephalomyelitis following acute infectious diseases, poliomyelitis, brain abscess and benign lymphocytic meningitis may be difficult to differentiate The differential diagnosis of these diseases is discussed under poliomyelitis and elsewhere in this text

In the acute stage of encephalitis the spinal fluid is clear, under normal pressure, without coagula, and there may be from 10 to 200 lymphocytes present The protein may be slightly increased, glucose is present in normal concentrations and the fluid is sterile on culture It is evident that these findings are of no diagnostic value.

In the chronic stage of encephalitis diagnosis can be made with confidence if there is present a parkinsonian syndrome (in a patient less than 50 years of age) with oculogyric crises, sleep reversal, disturbances of respiration or typical personality changes In some cases the differentiation from a progressive cerebral degeneration or tumor of the hypothalamus may require prolonged observation in order to establish the diagnosis

The mortality rate during the acute stage cannot be estimated. The development of late symptoms is of very bad prognostic import

Saint Louis Encephalitis (Epidemic Encephalitis Type B, American Encephalitis) The disease caused by the virus of the B group is different from the European form of the disease caused by virus A. In the United States it has occurred in the region of Saint Louis, Missouri

Encephalitis type B includes both the Saint Louis and the Japanese forms of this disease Clinically these types of epidemic encephalitis do not vary despite the detectable differences in the causative viruses

Epidemics and sporadic cases of encephalitis type B begin in July or August and decline rapidly during September and October The manner in which the virus is transmitted from one to another or from whence it came or where it goes is unknown

In comparison with encephalitis type A the process in type B is more severe and more generalized However, in type B there is no tendency to destroy selectively the substantia nigra and the oculomotor nuclei which is characteristic of type A In type B, in addition to the brain involvement, inclusion bodies are often present in the kidneys

The incidence has been most frequent and most severe in elderly residents of suburban and rural districts The incubation period is unknown

For convenience of description the manifestations of this disease, the onset, and the progress have been divided into types and stages These are more artificial than real because there is much overlapping and variation in the types of symptoms and the course of virus B infections

SYMPTOMS In general, there are restlessness and delirium beginning one or two days after the onset of the fever The sensorium is clouded and stupor or coma may ensue

In general the progress of type B infections consists of the prodromal period, which lasts 2 or 3 days, and the period of stupor and delirium, which may be present from 2 to 7 days However, great variations in duration of the symptoms may be observed. There are some cases in which the disease may be characterized by severe chills and coma, and life may be terminated within 24 hours In contrast to these fulminating instances of the disease, a few patients may have fever and stupor for months and eventually may recover. Despite these variations in symptoms and dura-

tion, usually the course of the disease lasts about 3 weeks, and terminates in full recovery without residua.

EXAMINATION. The findings on physical examination are dependent on the severity of the disease and on the duration and the trend of the disease at the time of examination.

On examination there are present intense symptoms Marked meningeal irritation, manifested by cervical rigidity, hypertonicity or often rigid musculature, tremors and fibrillary twitchings are present Trismus and transient cerebral palsies such as hemiplegia, monoplegia or bilateral paralysis may be revealed At this stage of the disease death may ensue from hyperpyrexia, paralysis of respiration and pneumonia. However, in some who have hyperpyrexia the fever declines, to be followed by a clearing of the sensorium, and convalescence ensues

After recovery there are never present more than a mild speech disorder, slight reduction in vision, deafness, gait disorder or slight psychic changes. Usually after recovery the results of examination are negative

During the active phases of the disease the leukocytes range between 10,000 and 35,000 per cubic millimeter, the increase is chiefly in the polymorphonuclear leukocytes; the lymphocytes are decreased

The spinal fluid is usually clear and the pressure is increased There are between 30 and 250 mononuclear cells per cubic millimeter The protein is increased and the globulin reaction is positive

DIAGNOSIS. During an epidemic the diagnosis is easily established by examination of the patient and the spinal fluid In sporadic cases the diagnosis depends on an awareness of the significance of an illness which has acute onset with high fever, delirium and restlessness or stupor, the signs of severe meningeal irritation, muscular rigidity, involuntary movements, and the changes in the blood and spinal fluid

In the Saint Louis epidemic in 1933 the mortality rate was about 20 per cent.

Equine Encephalitis (Epizootic Equine Encephalitis) Equine encephalitis is caused by two similar viruses. The western form of the disease occurs in western United States, and the eastern occurs in the region of the Allegheny Mountains and east to the Atlantic seaboard

Western equine encephalitis is a disease principally of horses and mules. The virus closely resembles that of the Saint Louis encephalitis (virus B).

Eastern encephalitis is a summer disease of equine and avian animals The eastern virus is similar to the western one and to the Saint Louis B virus but with differences known to those who have studied it Despite these differences in the viral characteristics, the diseases caused, irrespective of the particular viral etiology, are essentially the same disease clinically

In equine encephalitis the human and horse infections occur within the same district There is reason to believe that the several varieties of mosquitoes which act as vectors obtain the disease from a reservoir of encephalitis which is present in birds The disease is not necessarily transferred from horse to man, but horse and man get the disease from the same source A large epidemic has occurred in Minnesota and the neighboring western states and to the north in Canada Epidemics of the eastern variety of the disease have occurred in Massachusetts In that epidemic those affected were children and a mortality rate of 65 per cent was recorded

There are prodromata consisting of drowsiness and headache which subside. Several days later headache, vomiting, drowsiness, muscular rigidity, positive Kernig's sign, absent reflexes, plantar extension and high fever ensue. The polymorphonuclear leukocyte count may rise to 50,000 per cubic millimeter The spinal fluid is under increased pressure and the cells vary in numbers from several hundred to 1,000 or more per cubic millimeter

The duration of the disease is short If the patient survives, the symptoms are gone in 10 to 15 days

The diagnosis of equine encephalitis may be suspected whenever acute enceph-

alitis in humans appears in a district in which an epidemic among horses

The mortality rate is high. Residua consist of mental deficiency, speec and hemiparesis

Australian X Disease. The virus of Australian X disease produces le symptoms identical with those of virus type B encephalitis The disease epidemics during the warm season, January to April, in Australia, New Sou Queensland and Victoria. Boys less than 5 years of age are more commonl than other persons though adults may have the disease.

Epidemic Hiccough. Hiccough is a common symptom of epidemic en (type A) Epidemic hiccough may be related to or may be an abortive encephalitis (type A).

Epidemics of hiccough occur in autumn or winter. These epidemics ma or follow epidemic encephalitis (type A). The disease often affects men c age or older It rarely occurs during childhood. It is mildly contagious.

The first symptoms commence with mild coryza, low fever and slow pul a day or two the hiccough begins. The hiccough may last only one day persist for a week Neither complications nor sequelae follow.

Herpes Simplex. Herpes simplex is a common viral disease. The virus mentioned in connection with diseases of the skin, of the mucous memb the genitalia and of the eyes. Here it is considered as a cause of diseas central nervous system.

Pathologic changes occur in the cortex and subcortical white matter. There flattening of the convolutions with petechial hemorrhages in the brain and loc *widespread regions of softening There is considerable loss of ganglion cells, w* replaced by large collections of fat-containing cells and a few leukocytes In th borhood of the necrotic regions there is an increase in glial cells, many of w well as some neurons, contain intranuclear inclusions The meninges are conges

The onset of symptoms is sudden with fever and sometimes chills. Symp *increased intracranial pressure quickly ensue There are evidence of m* irritation and stupor of varying degree

In fatal instances, death has occurred between the eighth and twelfth da onset

On examination there are transient pupillary changes, alterations in paralysis and paresis of muscle groups, and abnormalities of sensation ir taste and smell Convulsions may occur. The cerebrospinal fluid shows a nuclear pleocytosis up to 1,000 cells per cubic millimeter, an elevated protei normal amount of sugar The white blood count reveals leukocytosis with *preponderance of polymorphonuclear cells.*

Herpetic meningo-encephalitis cannot be distinguished clinically from an form of viral meningo-encephalitis It has been diagnosed with certainty isolation from the brain, spinal cord or cerebrospinal fluid of herpes simple

Acute Benign Lymphocytic Meningitis (Virus). Choriomeningitis is mon acute disease which is self-limited and terminates in complete recover

The causative virus of choriomeningitis seems to be endemic in house mice an ... has been recorded in a place of residence free of mice a cor een d

incriminated as important natural vectors of any disease

Acute benign lymphocytic meningitis occurs sporadically and in small ep and most frequently affects children

The illness commences acutely with headache, fever and vomiting, me *irritation, irritability*, insomnia and intense restlessness. As a rule nystagmus, and paraplegia of the cranial nerves do not occur. The temperature ranges 102 or 103 F (38.9 or 39.4 C) and ends by lysis in about a week.

The spinal fluid pressure is increased The fluid is clear. The cell count ranges from 100 to 1,500 per cubic millimeter or higher Early in the course the leukocytes are predominant but later mononuclear cells constitute most of the total count. The sugar and chloride contents are normal, thus aiding in the differential diagnosis It is said that the pleocytosis may persist to some degree for weeks after clinical recovery has occurred, but as a rule the cell count returns to normal during the second or third week.

The diagnosis is based on the predominance of mononuclear cells and the absence of any demonstrable organisms, on the brief course and favorable outcome of the disease and on the absence of otitis, mastoiditis, septic sore throat and other infections. Abortive poliomyelitis may give rise to an identical syndrome

Rabies (Hydrophobia, Lyssa, Rage) Rabies is usually transmitted by the bite of a rabid (mad) dog, skunk, or any other animal infected with rabies

Emulsions of brain tissue from a rabid animal will contain the contagion of rabies after it has passed through a Berkefeld filter Therefore the cause of rabies is placed in the group of filtrable viruses

There are degenerative changes without definite evidences of inflammation in the lenticular nuclei, the thalamus, cerebellum and parts of the spinal cord In cases in which the incubation period is short, but the latent period is prolonged, the process may be almost entirely degenerative The characteristic features of the disease are Negri bodies, which are rounded structures between 4 and 10 microns in diameter, which stain with acid dyes, and are found in the cytoplasm of the nerve cells of the hippocampus, cerebellum, spinal ganglia and cerebral cortex

In only a few of those bitten by a rabid animal will the disease not develop. Whether or not the patient succumbs to the infection depends on the severity as well as on the situation of the bite or bites The infection develops most frequently when there are multiple wounds near the head

The *incubation period* in general is from 3 to 8 or 10 weeks It is shorter when the bite is on or near the head and longer when it is on the leg or foot Multiple bites increase the dose of the virus and thus shorten the incubation period In rare instances the infection remains latent in the nervous system for a year or more before giving rise to active symptoms The name hydrophobia refers to the painful spasms of the pharynx and larynx, which are precipitated by effort to take fluids The rabid dog, tortured by fever and thirst, may be found dead beside a stream where he fell with convulsions on attempting to drink water

Symptoms. The first symptoms are pain and numbness in the region of the bite Soon there are drowsiness, headache and loss of appetite The drowsiness is supplanted by restlessness and irritability In some there is no fever, in others the temperature may reach 105 F (40 5 C) Irrespective of fever, the patient begins to be frightened by noises and bright lights, the stimuli for which are of central origin. These annoyances increase and are supplanted by terror The patient stares and foams at the mouth in much the same way as does the mad dog

Examination Local twitchings followed by convulsions are frequent. Periods of delirium may alternate with periods of lucidity Cervical rigidity is severe and [illegible]

vulsions After 1 to 3 days the paralytic stage sets in It is characterized by coma and may be followed by death within a few hours

The spinal fluid usually shows a few lymphocytes In cases in which the incubation period is brief and the symptoms are acute, there may be several hundred cells in the spinal fluid.

Diagnosis The history of a dog bite or bite by mink, skunk or other carnivora followed by an incubation period of 3 to 10 weeks, and by the characteristic terror,

excitement and hydrophobia is definitely diagnostic. The shorter durations of the incubation period occur when the bites are sustained on the face or hand. The diagnosis of hydrophobia or rabies can and should be established by examination of the brain of the carnivora, if rabies is suspected, as soon as the bite is inflicted In most states examination of the brain of a rabid animal may be had from laboratories of the state department of health

Once the disease is established and symptoms have developed, death is inevitable

Preventive treatment is of the greatest importance. The wound is opened widely and thoroughly cauterized with phenol and alcohol The Pasteur treatment is given as soon as possible thereafter This treatment is the use of antirabies vaccine.

NEUROLOGIC COMPLICATIONS FOLLOWING THE USE OF RABIES VACCINE. The incidence of neuroparalytic accidents complicating the use of rabies vaccine in a world-wide statistical review is 1.5,814 in a series of 1,290,758 treated patients. In those who have adverse reactions there is a mortality rate of 25 *per cent*, an insignificant figure.

Pathologic changes include adventitial infiltration of cerebral vessels with round cells, perivascular microglial reaction and infiltration of the vagus nerve with polymorphonuclear leukocytes

There is the history of previous antirabies treatment, usually in childhood. During the course of prophylactic use of rabies vaccine there may be neuroparalytic disease such as a transverse myelitis or systemic reactions These reactions may occur at any time during or soon after the administration of the vaccine. Either death or recovery may follow

Encephalomyelitis Following Certain Viral Infections (Intoxication). Encephalomyelitis sometimes follows measles, German measles, smallpox, *mumps*, and whooping cough The etiology is essentially the same in all of these diseases, *namely, one or more filtrable viruses producing a series of toxins* which have a similar effect on the myelin

There are diffuse focal perivascular degeneration and demyelination.

SYMPTOMS The following syndromes occur: (1) meningism, symptoms referable to acute diffuse involvement of the cerebrum, (2) cerebellar syndromes, (3) spinal syndromes, (4) optic neuritis and (5) multiple focal and diffuse lesions of the brain or spinal cord It is well to recall that encephalopathies may follow acute and severe infectious diseases such as *diphtheria, pneumonia, septicemia, erysipelas*, scarlet fever, influenza, dysentery and malaria. *In some instances following encephalomyelitis it may well be that the complication of the viral disease by a bacterial* infection was responsible for the syndromes present

Meningism is characterized by a sudden rise in temperature up to 105 F (40.5 C) accompanied by drowsiness, stupor or even coma. There is evidence of meningeal irritation such as cervical rigidity, Kernig's sign and tache cérébrale. Headache, vomiting, dilatation of the pupils, and muscular twitchings appear within a few hours of the onset

The spinal fluid is under increased pressure and there is a moderate increase *in* the lymphocytic cell count The globulin and total protein content are moderately increased The illness is self-limited and quick recovery is the rule

When there is a sudden onset of violent convulsions at the height of the disease, [illegible] may disappear;

[illegible] esia below the

[illegible] oss of all reflexes [illegible] symptoms ap-

[illegible] attack of mumps

[illegible] igns of cerebellar ataxia, including loss

[illegible]

occur during the convalescence from measles or German measles. It most commonly follows varicella though nervous symptoms are rare in this disease. The cranial nerves may be involved and ptosis of the eyelids, squints, optic neuritis, retrobulbar neuritis, facial palsy and palsies of the bulbar muscles are described.

Deafness may represent the only evidence of involvement of the nervous system. Often hearing is suddenly lost without warning and no symptoms of irritation of the eighth nerve are present, but in other cases the onset is marked by tinnitus, vertigo, nystagmus, nausea and vomiting. Deafness may develop in children who have been exposed to mumps, and it is thought that deafness may occur without parotitis It has been estimated that nearly 5 per cent of all deaf mutes owe their condition to an attack of mumps in childhood.

The spinal syndromes have spinal cord manifestations like the acute ascending myelitis of the Landry type which has been mentioned in Chapter 6 The spinal syndrome may be complicated by convulsions and stupor indicating cerebral involvement.

Optic neuritis may occur during measles or German measles or soon thereafter. It at times follows vaccination for smallpox or occurs immediately after the rash subsides In some cases there is reduction of vision and even transient blindness as the result of congestion of the optic nerve.

During mumps the optic nerve may be affected Optic neuritis, neuroretinitis, retrobulbar neuritis, papilledema and optic atrophy have been reported Some of these conditions are the result of increased intracranial pressure.

Multiple and Diffuse Lesions of the Brain or Spinal Cord. There are lesions of this type which cannot be considered separately They occur sporadically in a number of diseases

Diagnosis The diagnosis may be suspected whenever in the course of an acute viral infection the patient becomes stuporous or delirious, and there develop convulsions and muscular rigidity, cerebellar symptoms, a spinal syndrome, optic neuritis or deafness. Meningitis, abscess of the brain and dural sinus thrombosis are the conditions most likely to resemble toxic encephalopathy During convalescence in certain cases ventriculograms will reveal symmetric wasting of the brain

If the neurologic symptoms are of brief duration, the prognosis is favorable for complete recovery If not, the prognosis must be guarded, for the patient may be permanently disabled.

TOXIC AND HEMORRHAGIC ENCEPHALOPATHIES AND THEIR SEQUELAE

Hemorrhagic encephalitis is a secondary process due to various toxins, bacterial and viral, and other poisons Any acute infectious disease may cause hemorrhagic encephalitis, but influenza is the commonest cause. Other infectious diseases also, such as scarlet fever, diphtheria, typhus fever, typhoid fever, malaria, pneumonia, septicemia and measles, may cause hemorrhagic lesions. Certain nonbacterial poisons, such as arsphenamine, carbon monoxide and hydrocyanic acid, may cause hemorrhagic encephalopathy

On examination of the brain there are seen small yellow or red regions which are most numerous in the centrum ovale, internal capsule, corpus callosum, brain stem and cerebellum

The manifestations may not be evident because the condition often occurs in stuporous or comatose patients as a result of the original infection. When it is possible

palsies are frequent

The diagnosis may be suspected but usually is not made clinically.

Cerebral Hemorrhage and Softening as a Sequela of Acute Infections. An infection may be followed by cerebral hemorrhage and softening. Pertussis, scarlet fever, pneumonia, diphtheria, measles, dysentery, influenza, typhoid fever and typhus fevers are among the commonest causes.

The onset commences with convulsions which are followed by hemiplegia, aphasia, hemianopsia or other focal cerebral manifestations. There may be stupor or coma. The spinal fluid is usually normal.

The diagnosis is made at postmortem examination.

SYPHILIS OF THE NERVOUS SYSTEM

The generic term neurosyphilis is employed to designate all forms of involvement of the nervous system by *Treponema pallidum* The term thus used includes all of the various types of neurosyphilis, and is made specifically applicable by an appropriate modifying adjective in each instance, for example, *meningeal*, wherein the various layers, especially the leptomeninges, show the most marked reaction; *parenchymatous*, wherein the brain or the cord is chiefly affected; and *meningo-vascular*, wherein both meninges and vessels are affected. Parenchymatous neurosyphilis is a general term, but through usage it has come to be employed specifically to designate degenerative and inflammatory processes of the substance of the brain and cord. Parenchymatous neurosyphilis finds its most precise meaning when employed for the description of tabes and general paresis and thus distinguishes these from other forms of neurosyphilis.

Meningeal neurosyphilis is manifested within the first, second, and up to the fifth year after infection It is thus a relatively early manifestation of tertiary syphilitic disease. Parenchymatous neurosyphilis, that is, tabes and paresis, is a late manifestation, appearing in from 5 to 15 or more years after the initial infection

Congenital Syphilis. Congenital syphilis is not hereditary, but is acquired in utero from a syphilitic mother The twenty-seventh Annual General Assembly of the International Union Against [illegible] postulates regarding the mode of transmission of [illegible] transmitted from the mother to [illegible] sage of spirochetes across the chorionic villi takes place after the fifth month of pregnancy. (2) Direct infection of the ovum by the sperm is unlikely. (3) The so-called spirochetal granules represent a developmental stage common to all spirochetes The assembly also recommended that the term hereditary syphilis be replaced by the term congenital syphilis

Levaditi and Vaisman, although in agreement with the foregoing postulates, have pointed out that Mayer reported 2 instances in which *Treponema pallidum* was found in the chorionic villi of aborted fetuses, one 4 months and one 3 months old. These, however, appear to be exceptional instances

Congenital syphilis of the central nervous system commences in the meninges and in perivascular spaces at the base of the brain. Acute syphilitic meningitis develops; localized regions of basilar meningitis may be present Infiltration by the infection invades the optic nerves and optic atrophy may ensue There are often endarteritis and infarctions of the brain, and if the subarachnoid spaces are obliterated, hydrocephalus ensues The foci in the meninges may become enlarged and organized and gummas may develop If the parenchyma of the brain is invaded and severely injured, general paresis results, or if the syphilitic process begins in the spinal meninges and affects the spinal nerve roots and the blood vessels and invades the cord, tabes will follow if sufficient destruction is wrought

A great many neurologists and syphilologists regard congenital neurosyphilis as [illegible] with con-

Often the attention of the physician is directed to the disease in either infants or juveniles by a knowledge that the mother has syphilis. In some instances the mother notices that the child is ill with what she thinks is a minor illness of the upper part of the respiratory tract (sniffles).

If the infant does not succumb to a meningitis, there will arise symptoms of various cranial nerve palsies. The seventh, third, fourth and sixth nerves are commonly involved A degree of hydrocephalus is present in about one third of all infants who have syphilitic meningitis Optic atrophy and blindness may follow hydrocephalus and papilledema or may appear spontaneously. Increased intracranial pressure may be present Hemiplegias develop suddenly as a result of thrombosis of the cerebral vessels. Apoplexy may prove to be fatal

In juvenile *paresis* there are dullness, apathy and forgetfulness. The child is untidy and careless of manners and dress. Grandiose trends, euphoria and speech defects develop The gait is clumsy and unsteady.

Juvenile *tabes* is less frequent than juvenile paresis. There may be no symptoms, and the condition is revealed by examination

Deafness beginning at 10 to 15 years is a common manifestation of congenital syphilis It is a nerve type of deafness and is bilateral and complete.

Convulsive disorders are common in the congenital syphilitic patient and may be the only symptoms of cerebral syphilis The convulsive seizures may be general or focal or may resemble the attacks of petit mal and grand mal of epilepsy

The serologic reaction of the blood or the spinal fluid is almost always positive unless the patient has undergone prolonged treatment.

The lesions of the *skin and mucous membranes* consist of rhinitis, bullous cutaneous eruption and abnormalities of the skin and hair

There may be pseudoparalysis as the result of acute osteochondritis. A congenital syphilitic infection may be present as osteitis and periostitis with frontal bossing of the skull, saber shin, scaphoid scapulas, saddle nose, scoliosis and osteomyelitis

In many the *second set of teeth,* the upper central incisors, show the peg shape and central notching described by Hutchinson (Hutchinson's teeth), and the molars may be beset with extra facets

The spleen and liver are sometimes enlarged and jaundice and ascites are present (see Diseases of the Liver, Chapter 13)

Interstitial keratitis may be present in both eyes, or iritis may be found without keratitis

The Argyll Robertson pupil is commonly present in neurosyphilis of all types. The pupils are usually unequal and irregular They do not react to light stimulation but do contract during accommodation. This type of pupil is usually bilateral but may be unilateral Its presence does not indicate active syphilis, for once developed, it is permanent whether the syphilitic process is arrested or not

Diffusely and widely dispersed retinitis and chorioretinitis appearing as small brown and yellow spots scattered over the entire retina are almost diagnostic, and are definitely so if associated with interstitial keratitis

In juvenile paresis the serologic reactions are strongly positive in both blood and spinal fluid The spinal fluid contains an increased number of lymphocytes. Results of globulin tests are positive The gold curve is often of the paretic type

In juvenile tabes the patient is 10 to 15 years of age. On examination Argyll Robertson pupils, optic atrophy, loss of knee and ankle jerks, positive Romberg sign and ataxic gait are present Serologic reaction of the spinal fluid is positive but the cell count may be low

The diagnosis of congenital syphilis may be presumed if there is present a family history of abortions and stillbirths, evidence of congenital syphilis in siblings, and a personal history of infancy with reference to prematurity, bullous cutaneous erup-

tions, rhinitis, bone lesions (roentgenograms), and positive serologic reactions of the blood and spinal fluid.

Acquired Syphilis. The term neurosyphilis is particularly appropriate in acquired syphilis since all of the tissues of the nervous system are affected. At times the infection progresses slowly enough that it becomes manifest in some particular part of the nervous system and thus originates one or more of the syndromes of the central nervous system which characterize neurosyphilis. The predominant affection of certain structures justifies the enumeration of the varieties, for instance, gumma, syphilitic endarteritis, meningo-encephalitis, meningomyelitis and syphilitic neuritis.

The *gumma* is a round, irregular, nodular granulomatous growth, varying in size and numbers. Single gummas, however, do occur in the region of the motor cortex The gumma is hard and frequently caseated in the center. The accumulation of gummas on a blood vessel occasionally obliterates the lumen of the vessel and creates a *syphilitic endarteritis* The artery may rupture and hemorrhage may ensue. When the vessel wall is weakened sufficiently, aneurysmal dilatations occur Partial or complete obliteration of the lumen of a vessel results in localized anemia and secondary softening of the tissues distally in the path of the vessel Gummas obliterate the lumen of a blood vessel by a proliferation of the endothelium of the vessel and replacement of the muscular and elastic fibers The endarteritic or obliterative process may involve only one or a few vessels or be very widespread The circle of Willis is frequently the seat of syphilitic endarteritis The veins (syphilitic phlebitis) reveal somewhat the same process that is observed in the arteries

Syphilitic meningitis may be gummatous and involve the dura mater or the leptomeninges either at the base or at the convexity of the brain All the nerves at the base may become involved, but particularly the optic and oculomotor nerves. Meningitis of the convexity may originate a *meningo-encephalitis* The meningitic process may be grossly circumscribed

Symptoms The symptoms of neurosyphilis may commence slowly or may appear suddenly When the symptoms develop slowly, the patient may complain of mild or severe headache which is possibly worse at night. There is dizziness and occasional vomiting Scattered pains and areas of numbness, or numbness of an entire member, and other subjective sensations are common Often the patient seems to be neurotic because of prevailing irritability, restlessness, anxiety, depression, apathy, dullness, mild or severe memory defects, and alteration of personality With the suddenly developing symptoms there may be attacks of unconsciousness, and epileptic convulsions. The fits may be of the jacksonian type, or may be a generalized convulsive disorder In a middle-aged adult the occurrence for the first time of a fit is suggestive of syphilis of the brain or a brain tumor. In the severest brain involvement mild or high-grade dementia, and varying degrees of stupor up to coma, alternating with delirium, excitement or violence, are present. The symptoms may be those of a suddenly appearing psychosis which has nothing distinctive about it.

Polyuria and polydipsia (diabetes insipidus) may be present, these follow involvement of the floor of the third ventricle and the tuber cinereum

Paralytic symptoms, as the direct result of cerebral softening from a syphilitic process, generally come on in early middle age. The absence of cardiac lesions, antecedent infections, or other diseases of the brain in young persons frequently points to the syphilitic character of the hemiplegia While the onset and progress may simulate hemiplegia of atherosclerotic origin, the mentality or higher cerebral functions are frequently intact in syphilitic hemiplegia.

Examination. Owing to the fact that the syphilitic process is most marked at the base of the brain, *cranial nerve palsies* are very commonly present Involvement of the optic and ocular nerves, especially the oculomotor nerve, is the commonest manifestation of syphilitic encephalitis. The ocular palsies are generally lower motor

neuron palsies As such the oculomotor nerve is severely involved, giving ptosis and external strabismus with diplopia and convergence The pupillary reaction to light is lost. A fixed rather than an Argyll Robertson pupil is characteristic of meningovascular neurosyphilis. The pupils are frequently irregular, dilated and unequal. The paralysis of the fourth and sixth nerves results in palsies of the superior oblique and external rectus muscles. The ocular palsies are generally unilateral and often are permanent.

Often there is a neuritis of the optic nerve which is most commonly unilateral in the beginning. Transient amaurosis, impaired vision, scotoma, contracted fields, hemianopsia and blindness, the results of syphilitic optic neuritis, are often present.

Anosmia, trigeminal neuralgia, neuroparalytic keratitis, facial paralysis, deafness, and paralyses, when present, of the palate, pharynx, larynx, sternocleidomastoid and trapezius muscles and the tongue are manifestations of an involvement of the cranial nerves or nerve

The physical findings of syphilitic hemiplegia differ in no wise from the signs of hemiplegia from any other cause.

The spinal fluid usually shows an increase in the number of cells, from 10 or 20 up to many hundreds, an increase of globulin, and positive serologic reactions. The colloidal gold test gives an ascending or luetic curve.

DIAGNOSIS The diagnosis of neurosyphilis can generally be based on the history, on the multiplicity and dissemination of the signs and symptoms, on the presence of pupillary signs, on the positive serologic reactions, and on the results of therapeutic tests.

General Paresis (Parenchymatous Neurosyphilis) General paresis is a chronic syphilitic meningo-encephalitis characterized by atrophy of the convolutions of the brain in the frontal, parietal and insular regions. There is a deepening of the sulci and flattening of the gyri Despite an increased vascularization, the cortex atrophies and there are both an internal and an external hydrocephalus The dura and the piarachnoid are thickened and adherent. There are a generalized proliferative glial reaction and disappearance of the ganglion cells. The inflammatory reaction and perivascular cellular infiltration extend into the substance of the brain Regions of softening secondary to periarteritic and endarteritic changes are scattered through the brain. Degenerative changes occur in the basal ganglia, in the brain-stem nuclei, especially those of the oculomotor nerves, and in the cerebellum The lateral and posterior columns of the cord are frequently degenerated Degeneration of the optic nerves and involvement of the posterior columns, when present, link general paresis with tabes and frequently constitute the basis for the presence of symptoms referable to both the spinal cord and the brain

SYMPTOMS The patient is more frequently irritable than euphoric, shows bad temper, lacks power of concentration, and is easily fatigued. There may be anxiety, insomnia and hypochondriacal complaints Loss of interest is common

There is often loss of appreciation of the correct ethical, moral and esthetic standards. A previously honest person may commit petty thefts, a hitherto sober person may indulge in excessive amounts of alcohol, or a moral person may become immoral. There is carelessness of personal hygiene. The manners deteriorate, the conduct becomes lax, and there are loss of interest in business and neglect of the usual responsibilities As the memory defect increases, details are overlooked and mistakes are forgotten Changes in temperament and often an unwarranted feeling of well-being develop

A general euphoria consisting of a sense of well-being, elation and exuberant phantasy may prevail. There is a meaningless incoherence in association of ideas. Interspersed among all of these feelings of grandeur are irritability and insomnia Manic outbreaks occur during which the patient may commit personal violence and

destruction or may destroy the property of others. The psychosis may simulate the Korsakoff variety, that is, with much chatter and then delirium. In some there is a depressive type of psychosis characterized by hypochondriacal ideas or delusions The depressed paretic expresses self-accusatory ideas and feelings of insufficiency. Often when there is sufficient destruction of the cerebral cortices, the patient becomes quiet, harmless, and demented and thus lives for a long time.

A convulsive disorder and apoplectiform paralytic attacks are two of the most characteristic manifestations of paresis The convulsion may be partial and may occur in any part of the body The face is most commonly affected by such a convulsion Localized twitchings, tremors, or other abnormal involuntary movements may persist for days or even weeks A rise in temperature may accompany the fits. The fits are sudden, are mild or severe, and may last from a few minutes to half an hour They may come on singly or be repeated and may pass over into status epilepticus and end in death

The apoplectiform attacks, of fleeting time interval, may give rise to partial or complete paralysis or to hemiplegia Paretic hemiplegias usually, at least the first ones, disappear in a few hours or days but in time the paralytic attacks leave permanent residua

The course of general paresis as a rule progresses slowly, with or without remissions The disease may begin suddenly, however, with a manic attack or epileptiform convulsion, and progress rapidly Generally all signs and symptoms become aggravated, and mental and physical deterioration progresses Speech is difficult and unintelligible; walking becomes awkward and finally impossible, the patient takes to the bed; incontinence of urine and feces sets in; complete dementia supervenes; and finally death occurs *but not soon enough*.

EXAMINATION. On examination the patient appears and acts silly The presence of pupillary changes is a most important finding The Argyll Robertson pupil is common in paresis, being present in about half of those who have this disease. As the disease advances, almost all have pupillary disturbances, and finally the pupil may be fixed and *respond to neither light nor convergence* A *completely normal* pupil, however, may be present in paresis Ocular palsies and optic atrophy with transient blindness are sometimes present.

Soon there is impairment of memory for recent events which is a part of a defect of the general mental processes Characteristic of this sort of intellectual defect is failure to appreciate ethical, moral and esthetic standards.

The speech is tremulous and dysarthric, an explosive sort of utterance emitted with a shower of slobbers There is slurring of letters and syllables Test phrases, such as "round the rugged rock the ragged rascal ran" are poorly repeated, or forgotten before they can be repeated. A fine tremor is present on the lips, tongue and eyelids, and there is a coarser tremor of the fingers *The handwriting is tremulous* and inaccurate. The deep reflexes are generally increased, frequently unequally. Spinal cord changes are indicated by signs of involvement of the posterior columns, and the clinical syndrome then becomes one of *taboparesis* In taboparesis the knee jerks and ankle jerks are absent There is swaying in the Romberg position Finally urinary incontinence ensues

The serologic reactions of the blood and spinal fluid are positive in practically all instances of the disease. In the blood the reactions may be negative early in the course of the disease or after "adequate treatment," so that negative serologic reac[illegible] do not exclude paresis The spinal fluid generally shows an increase [illegible] an increase in globulin. [illegible] "paretic" curve. [illegible] nbination of symptoms [illegible] tive serologic reactions of the blood and spinal fluid or the spinal fluid alone, permits of the diagnosis of

general paresis in most instances The diagnosis of general paresis can rarely be made in the absence of positive serologic reactions.

Spontaneous recoveries or remissions have been reported The average duration of the disease is about 3 years The disease is always fatal in the advanced stages.

INFECTIONS OF THE NERVOUS SYSTEM BY HIGHER PLANT ORGANISMS

Various members of the higher plant organisms which cause disease of men and animals may reach the nervous system during the course of the infection and thus originate disease. The organism *Torula* (*Cryptococcus neoformans*) is the only one expressing special tropism for the nervous system.

Torulosis (Cryptococcosis). The organism *Torula* (*Cryptococcus neoformans*) of a genus of yeastlike fungi, reproduces by budding Several types are recognized which are differentiated by their morphologic differences The organism enters the body through the upper part of the respiratory system and thence passes to the nervous system

The brain shows at necropsy a granulomatous meningitis most severe at the base and very similar to tuberculous meningitis The fluid in the subarachnoid spaces is turbid and gelatinous, and contains the organisms in large numbers. In the cortex are found cysts and granulomas The organisms penetrate along the perivascular spaces into the cortex from the subarachnoid space They then proliferate, distending the tissues and forming small cystic structures filled with a gelatinous material composed of the organisms and their capsules There is practically no reaction by glial and nerve cells. Lesions may be found deep in the cortex and basal ganglia which seem to have arisen as a result of embolism.

Evidences of the disease outside of the nervous system are rare. Involvement of the lungs is sometimes seen. The lymph nodes may be enlarged. In generalized torula infection the organisms may be found in the blood and urine, and the liver and spleen may be enlarged Torulae have been found in pus withdrawn from the liver and in cultures from the pharynx, tonsils and nasal sinuses A torula infection may be associated with or resemble tuberculosis, and during life it may be very difficult to distinguish the two processes

Torula infection may occur at any age or in either sex Symptoms commence with vomiting and drowsiness In children the head may enlarge slowly as a result of hydrocephalus In some instances there is low-grade fever. In others the disease progresses without signs of infection or systemic symptoms but a slow failure of health ensues.

Cervical rigidity and Kernig's sign are present but they are not so severe as in purulent meningitis. Hemiplegia or hemiparesis and other evidences of focal cerebral lesions may be evident on examination Papilledema is usually present and may eventually lead to optical atrophy and reduction of vision The sixth nerves are frequently paralyzed and the other cranial nerves are sometimes involved. Anemia may be absent but sometimes develops in profoundly cachectic patients. A slight increase in the leukocyte count may be present.

The spinal fluid shows a cell count from 50 to 1,000 per cubic millimeter. Mononuclear cells predominate but leukocytes may be present. Many torulae usually are present and are recognized by their refractile capsules Cultures are usually obtained on Sabouraud's medium Torulae may be absent from the spinal fluid or may fail to grow on Sabouraud's culture media

The diagnosis cannot be established without demonstration by culture of the organism in the spinal fluid The disease clinically resembles tuberculous meningitis. If the intracranial tension is high, sarcomatosis of the meninges or brain abscess may be present. Effective treatment is not known.

DISEASES OF THE BRAIN DUE TO TRAUMA

In head injuries there are: (1) the element of shock or concussion, (2) the signs of increased intracranial pressure and (3) the evidences of destructive lesions in the brain. As time passes, the signs and symptoms of such sequelae as abscess of *the brain, meningitis, subdural hematoma*, effusions into the subdural or subarachnoid spaces, delayed hemorrhage and pneumocephaly are recognized if they arise.

A history of a fall and head injury in a patient who has fits or headache or both and who is first examined long after the injury occurred is difficult to evaluate, for all patients have had degrees of head injuries in the past In the stoic person it is safe to assume there was injury to the brain if the patient was unconscious for an hour or more immediately after the accident. A history of vomiting, convulsions, paralysis, bleeding from the ears and roentgenologic evidence of fracture of the skull are often conclusive

Extradural Hemorrhage. Hemorrhage between the skull and the dura is termed an extradural hemorrhage The significant manifestations of an extradural hemorrhage are a history of head injury with or without loss of consciousness, followed by a period of time during which the sensorium was clear, and then rapidly increasing signs of intracranial pressure. If focal signs such as dilatation of the homolateral pupil and hemiplegia or muscular twitchings on the opposite side are present, localization of the hemorrhage is largely accomplished. Roentgenologic examination of the head is diagnostic in many instances

The prognosis is unfavorable if operation is not performed at once. In the severely injured patient a life may be saved by operation but the patient may not be grateful because of the limitations the injury imposed on locomotion

Subdural Hematoma. This hematoma is considered in all cases of unexplained cerebral symptoms following injuries of the head, particularly if there is increased intracranial pressure, unless some other cause is apparent. The conditions which resemble subdural hematoma are brain tumor, cerebral abscess, hydrocephalus and subarachnoid hemorrhage. *If subdural hematoma is suspected, puncture of the subdural space* will usually either establish or disprove the diagnosis If a hematoma is present blood will be obtained from the exploratory needle.

Chronic Subdural Hematoma. Chronic subdural hematoma is often caused by trauma. It can occur spontaneously. Trauma on forehead or occiput without indications of concussion may lead to rupture of cortical veins. From this rupture blood leaks into the subdural space and forms a collection in this space, over the convexity of the brain, and often bilaterally

Chronic subdural hematoma was formerly believed to be an inflammatory process known as chronic pachymeningitis hemorrhagica, found in demented, epileptic, tabetic and alcoholic persons. It is now known to be traumatic, and it occurs in the types of patients enumerated because they fall down and injure their heads, and they are less able to give a history of trauma

There is a latent period after the injury of days to months before symptoms appear Headache develops and increases in frequency and severity. Intermittently there may be drowsiness, forgetfulness and at times confusion which may progress to stupor, or even to coma The pulse rate tends to become slower, falling to 60 or even 50

In all cases of rapidly developing intracranial pressure, without clear localizing [illegible] slowness and confu-
[illegible] story of *head injury*
[illegible] without a history of
head injury of some degree

Pneumocephaly and Cerebrospinal Rhinorrhea. The terms pneumoventricle, pneumocranium, intracranial aerocele and pneumatocele refer to the *accumulation of air within the cranial cavity*. This occurs in a patient who has sustained a fracture at the base of the anterior fossa of the skull. A fissure in the bone extending through the frontal sinus may be palpated. Some weeks after what was considered to be a minor injury headache, vomiting and other signs of increased intracranial hypertension ensue. The signs of intracranial hypertension may commence and persist soon after the head injury.

The flow of fluid from the nose is characteristic of this condition. The fluid is clear, blood-stained or even yellow. Sometimes large amounts of fluid are discharged at intervals but in other cases there is a constant drip.

The demonstration of air within the cranium by roentgenologic examination is conclusive The diagnosis may be suspected if head injury has been followed by discharge of fluid from the nose and increasing manifestations of increased intracranial pressure

The outlook depends on the degree of injury and on the outcome of prompt, skilful surgical treatment.

Spontaneous cerebrospinal rhinorrhea may occur in which there is no evidence or history of trauma to the head. Such rhinorrheas are due usually to imperfections in the bony structures at the base of the brain.

DISEASES OF THE BRAIN DUE TO CIRCULATORY DISTURBANCES

The circle of Willis gives origin at the base of the brain to vessels which pass through small perforations in the occipital bone to enter the brain substance, and to larger vessels which pass from the main trunk (basilar and posterior cerebrals) of the circle to continue their course over various surfaces of the brain within the pia mater, branching and being progressively dispersed into smaller vessels which disappear within the sulci, enter the superficial gray cortex and continue into the white matter. The internal carotid arteries and their branches supply the rest of the brain.

The vessels of the dura mater and pia mater, the intracerebral vessels, and the choroid plexus are supplied with vasomotor nerves. The vessels of the brain act anatomically and physiologically as vessels act elsewhere in the body. Stimulation of the cervical sympathetic trunk results in contraction of the pial vessels Stimulating the vagus dilates the capillary bed

The caliber of the intracranial arterioles is influenced by chemical substances (carbon dioxide, chlorides and epinephrine) in the blood stream and vasomotor nerves and by variations of venous pressure and pressure of the cerebrospinal fluid.

The rise in pressure within the veins causes stasis of blood. If the rise in pressure is slow and not too great, vasodilatation results, thereby overcoming the venous stasis caused by increased venous pressure If the rise in cerebrospinal fluid pressure is sudden and great, a rise in systemic arterial pressure is necessary to overcome the venous stasis (see Intracranial Tumors, p. 1181). This rise of systemic arterial pressure subsequent to increased intracranial tension is accompanied by slowing of the pulse and respiratory rates If the intracranial tension becomes too great, paroxysmal irregularities of respiration ensue.

Cerebral Anemia. Cerebral anemia may occur acutely or chronically in myocardial weakness and decompensation, or in acute dilatation of the heart and in severe degrees of general anemia

Acute cerebral anemia results from sudden pressure on the vessels of the neck (carotid sinus syndrome), rapid loss of blood, and sudden dilatation of the splanchnic circulation which may follow withdrawal of large amounts of ascitic fluid or pleural effusions.

The symptoms of acute anemia of the brain are apprehension, scotomas, giddiness, weakness and faintness, and often syncope. Sudden loss of large quantities of

blood, as from postpartum hemorrhage, rupture of tubal pregnancy and a bleed peptic ulcer, has resulted in complete and permanent cerebral deterioration a blindness due to ischemia of the ganglion cells of the retina, and subsequent atrop of the nerve fibers.

Chronic cerebral anemia is often due to a chronic anemia caused by a gr reduction of erythrocytes In cerebral arteriosclerosis intermittent transient peric of local or general anemia appear when posture is suddenly changed. In those w have orthostatic hypotension the general circulatory apparatus and the local vasc lar bed can no longer compensate for the sudden effects of gravity during postu changes Cerebral anemia may be incident to sudden changes of position by one wl has been long confined to bed.

The symptoms of chronic cerebral anemia may be headaches, dizziness an faintness, especially severe on sudden shift of position of the head. There may be deficiency of memory and increase in irritability.

On examination usually there are no local focal cerebral signs The diagnos is made because of the presence of generalized and retinal arteriosclerosis

Cerebral Hyperemia. Cerebral hyperemia is a part of all acute inflammato and toxic encephalitides, failure of the right side of the heart, polycythemia, mali nant hypertension and partial obstructions of the dural sinuses, jugular veins superior vena cava When a patient who has pulmonary emphysema with increase venous pressure lies down or bends forward there may be cerebral hyperemia Whe a person who has atherosclerosis or arteriosclerosis bends forward or lies down th vessels lack the ability to make the normal adjustments, and therefore there ar transient giddiness, general tingling, suffusion of the face, and headache In malig nant hypertension an increased intracranial tension may be permanently increase because of cerebral edema with multiple small hemorrhages and softenings, an constant headaches and choking of the optic disks develop This condition of hyper tensive encephalopathy, which often occurs in malignant hypertension, of Wagene and Keith, is distinguished with difficulty from that caused by intracranial tumor if multiple focal signs, due to arteriosclerotic softenings, are not present.

Edema of the Brain. A generalized cerebral edema is often a part of a anasarca as in congestive heart failure or edema caused by decreased concentration of serum proteins, starvation and generalized sepsis Focalized cerebral edema sur rounds abscesses, hemorrhages and tumors. At necropsy the brain is large and pale

The symptoms of cerebral edema consist of mental and motor apathy, menta confusion and, perhaps, focal or generalized convulsions The pulse is slow and the respirations are irregular and often periodic in character. The systolic blood pressure is usually raised above its usual level (160 to 170 mm of mercury). The stupor may increase and coma and death may ensue

Arrest of Cerebral Circulation. Arrests of cerebral circulation from cardiac arrests cause anoxia and neuronal damage Successful cardiac massage performed by surgeons for cardiac arrest during surgical procedures has been limited to cases in which the critical time limit of 5 minutes has not been exceeded. Premortem and postmortem studies of cases in which the heart has restarted after periods longer than 5 minutes are scarce.

Three British investigators, Howkins, McLaughlin and Daniel, reported an instance in which total duration of cardiac arrest was computed at 10 to 11 minutes until re-establishment of the heart beat by massage Six hours postoperatively abnormal neurologic responses were present and at 10 hours the patient's condition resembled somewhat that of decerebrate rigidity, but the patient survived 26 days. During this period the coma remained at the same depth, the patient responding only to strong painful stimuli The deep reflexes and the degree of hypertonia varied from day to day. Features of clinical interest included (1) a coma which was pe- ... in that the brain stem was rather active although higher cerebral activities

were depressed, (2) "seizures" occurring 8 days after operation, (3) absence of reaction to menace despite the presence of pupillary reflexes and spontaneous ocular movements, (4) failure to respond to auditory stimuli, (5) atrophy of the small muscles of the hand indicating considerable change in the anterior horn cells, (6) normal results in examination of spinal fluid and (7) almost straight lines in electroencephalograms with complete absence of any alternating potential difference. The patient died 26 days after operation of pneumonia and infection of the urinary tract.

Necropsy revealed excess fluid in the subarachnoid space. The sulci of the brain were widened Section of the brain revealed a moderate generalized ventricular dilatation, outer pallor and a slight generalized diminution of the thickness of the cortex and irregular areas of pallor of the basal ganglia. Microscopic examination revealed the disappearance of the majority of the pyramidal cells of the cerebral cortex and an increase of astrocytes and microglial proliferation, especially in the occipital cortex. The destruction of the occipital (visual) cortex and the superior temporal gyrus was severe.

Arterial Malformations and Aneurysms. Arteriovenous aneurysms and saccular aneurysms occur in association with the arteries of the circle of Willis (posterior group) and the carotid arteries (anterior group). These lesions are often of millimeter dimensions and produce symptoms only if they enlarge, leak, or rupture.

Aneurysms of congenital origin of the cerebral vessels occur between the ages of 30 and 50 years Aneurysms of atheromatous origin occur in persons more than 50 years of age Cerebral aneurysms occur in young or middle-aged adults although children may be affected Women are more frequently affected than men

Congenital arteriovenous aneurysms are often situated on the lateral surfaces of the hemisphere in the distribution of the middle cerebral artery but may occur in any location The walls of the dilated vessels are often partially calcified and degenerated, and thrombosis is common

The available information on 150 instances of subarachnoid hemorrhage, almost all in members of the armed services, has been recently reviewed by Magee He could not find any reliable premonitory sign of aneurysm or its rupture There was no evidence that physical strain was a cause for rupture In most cases the symptoms appear suddenly and the victim becomes stricken without premonitory warning

In the majority of those who have subarachnoid hemorrhage violent headache is the most important presenting symptom This usually is accompanied by moderate pyrexia, vomiting and rigidity of the neck which in many instances lead to the suspicion that meningitis is present In Magee's series vascular hypertension rarely was found; positive serologic reactions for syphilis were not obtained in any cases

The gravity of subarachnoid hemorrhage is well illustrated in Magee's series in which the mortality rate was 56 per cent Of his 150 patients 105 either died or were seriously crippled by paralytic sequelae (hemiplegia), incapacitating headache or vertigo. A second hemorrhage occurred in 50 of the 150 patients, and this represents an even graver prognosis when it is realized that 52 of the 150 died in the primary attack. The 50 recurrences therefore occurred among the 98 survivors of the first attack The prospects of good recovery diminished with advancing years; few of those examined subsequently to an attack were entirely free from symptoms Necropsy in 58 of the 84 fatal instances of the disease disclosed 43 ruptured aneurysms, these were commoner in the anterior half of the circle than in the posterior half and on the right side than on the left. The latter observation is the reverse of that commonly found in intracerebral hemorrhage of other varieties, the cause is obscure.

The cerebral aneurysms of atheromatous origin cannot be differentiated from the congenital ones prior to necropsy

Cerebral aneurysms may arise from causes other than congenital malformations or arteriosclerosis Syphilis, mycotic aneurysms and those of periarteritis nodosa

as well as those arising from penetration of the vessel wall by infections occur, but these causes are not common.

Often cerebral aneurysms are accidentally discovered at necropsy when there had been no recognized symptoms during life In some the aneurysm is manifested only on rupture with massive, often fatal, ventricular or subarachnoid hemorrhage. In still others there may be a history suggestive of small ruptures or leaks The patients recover from the apoplectic effects, but the subsequent course is associated with further ruptures until a large hemorrhage ends fatally.

In some instances the enlargement or leakage of the aneurysm will produce focal or general convulsions. There is a sudden onset of severe headache, vomiting, loss of consciousness, slow pulse, periodic breathing, and often convulsions If there is a moderate hemorrhage, the patient may remain unconscious until death a few days later During this period the head may be retracted, the legs and the arms fully extended, the legs adducted and the forearms pronated Convulsive twitchings of the entire body, irregularity of respiration and vomiting are frequent Kernig's sign, photophobia, hyperesthesia and herpes zoster are often present. Some patients survive and, after the acute symptoms are over, usually show mental deterioration

There is usually fever, the temperature rising to 104 F (40 C) In some instances the patient complains of a noise in the head. Each seizure is followed by transient weakness or paralysis of the extremity in which the convulsion begins. However, in those who have these early symptoms, complete recovery occurs until a persistent hemiplegia ensues With the motor symptoms there are hemianopsia, aphasia and other cerebral symptoms.

Leukocytosis is present. The cerebrospinal fluid contains blood Clotting does not occur on standing The color is pink or red during the first day but soon begins to turn yellow, brown or orange The diagnosis cannot be made until there has been some leakage of blood into the cerebrospinal fluid

Leakage of an intracranial aneurysm is compatible with life Some of these patients have a permanent hemiplegia after one or more leakages have occurred

Rupture of an intracranial aneurysm is fatal almost at once

Arteriovenous Aneurysm of the Carotid Artery. Arteriovenous aneurysm of the carotid artery in the *cavernous sinus* may be due to traumatic communication between these two structures, often as the result of a skull fracture However, these lesions, like those in the region of the circle of Willis, may be of congenital origin and occur in the same age groups of patients as do lesions of the circle of Willis. Occasionally the condition may develop as a result of atherosclerosis in persons beyond middle age.

Immediately after traumatic injury there is an audible bruit within the cranium which often can be heard without the aid of the stethoscope The orbital tissues become edematous and the veins about the orbit, distended The eyeball protrudes and there is palpable and visible pulsation synchronous with the heart beat

The diagnosis is made on the basis of a history of trauma, exophthalmos and pulsation of the eyeball. Defects in the superior orbital plate will cause pulsating exophthalmos. Various types of congenital aneurysm and hemangiomas will give rise to the same symptoms These conditions are distinguished by the absence of trauma Thrombosis of the cavernous sinus causes exophthalmos but not pulsation or an audible bruit. Pressure on the affected artery in the neck will stop the bruit and reveal the side of the lesion

Ligation of the internal carotid artery is recommended and usually results in great improvement, if not in cure, of the condition

Intracranial aneurysm of the carotid artery occurs at all ages but most commonly in young and middle-aged women.

Aneurysms of the nontraumatic type may be either fusiform or pedunculated. These aneurysms invariably are filled with blood clots, and there are adhesions

around the lesion where leakage or rupture has occurred. Staining of the subarachnoid and a subdural space with blood pigment is almost constantly observed. Subdural hematomas may be present.

Ocular signs and headache are constantly observed in those lesions affecting that part of the carotid artery which is inside the skull before it divides into the middle and anterior cerebral arteries. Within an anatomic radius of about 1 inch (2 5 cm) around this part of the carotid artery lie the optic, oculomotor, trochlear, abducens and trigeminal nerves, which may be injured by these aneurysms

In instances of aneurysms of congenital and arteriosclerotic origins increase in size of the expanding segment of the carotid artery is attended by prodromes of the impending disaster. These prodromes consist of headache and vertigo. When the aneurysm ruptures, the patient has a sudden sharp headache and pain in the eye, hears loud noises, and falls unconscious Slowly the eye begins to protrude, pulsating synchronously with the heart beat. Pulsation may not begin, however, for some months after the onset of exophthalmos. The exophthalmos is exaggerated by increase of intracranial pressure. The ocular veins are dilated and edema of the soft tissues about the orbit ensues.

The eye is observed to be forced laterally and rotated outward and down but it can be easily pushed back into the socket, a procedure which causes pain. The eyeball may recede into the orbit if compression is exerted on the carotid artery. Dilatation of the facial veins which drain into the ophthalmic vein may be present Auscultation over the eye or over the head will disclose a bruit which is discontinued by carotid pressure.

The prodromes consisting of headache and vertigo do not always immediately end in disaster. In such instances the oculomotor nerve is the most commonly damaged, and hence an early oculomotor palsy is often present. Pressure or irritation in this region causes pain in the ipsilateral eye, eye socket, and forehead and often along the side of the nose and inner canthus

The upper lid is observed to be ptosed and covers the pupil so as to obscure vision, the eye turns outward, and the pupil is dilated and does not react to light or convergence or consensually. A slight ptosis of the upper lid, with only an appreciable dilatation of the pupil, is the minimal sign of dysfunction. Occasionally the pupil on the involved side will be smaller than the pupil on the opposite side. Extraocular paralysis may occasionally be present Sometimes an episodic type of paralysis occurs which suggests multiple sclerosis or perhaps myasthenia gravis An associated involvement of the fourth and sixth cranial nerves is often observed.

Papilledema may be caused by direct irritation of the tissues about the optic nerve or it may arise from increased intracranial pressure.

If there is bleeding into the subarachnoid space, the symptoms of spontaneous subarachnoid hemorrhage occur, such as meningismus, mental confusion, or long-continued stupor. Vomiting may be an early symptom.

Immediately after the onset of symptoms there are often fever and leukocytosis Roentgenograms of the skull or orbits may reveal calcification situated under the bones or deep in the substance of the brain when intracranial aneurysms are present.

Ligation of the internal carotid artery has been successful in treatment in some of these patients.

Cerebral Arteriography. Arteriography may be used in cerebral vascular syndromes as an aid in the differential diagnosis of hemorrhage from thrombotic softening Arteriography will facilitate the decision of whether or not surgical intervention should be performed in cases of hemorrhage. It is barely possible that occasionally arteriography would make possible treatment with vasodilators in partial or complete thrombosis of the cerebral artery occurring at its termination or, more frequently, at the carotid bifurcation.

This procedure in the diagnosis of cerebral aneurysms and angiomas is safe in

experienced, trained hands, and should be practiced whenever aneurysms or angiomas are suspected It is a guide for the neurosurgeon and an aid in deciding whether surgical intervention should or should not be performed. Arteriography of cerebral tumors is limited to the cases in which the symptoms suggest vascular tumor (meningioma) and to cases of temporal tumor in which ventriculography is not feasible or its interpretation is difficult because of displacement of the ventricular system In cranial trauma arteriography is less indicated than ventriculography

Arteriosclerosis of Cerebral Arteries. The two main varieties of cerebral arterial disease are atherosclerosis or atheroma and arteriosclerosis. These have been described under vascular diseases.

Atherosclerosis and Arteriosclerosis. *Atherosclerosis* in the arteries of the brain is a process identical with that which occurs in the large arteries of the heart. It consists of a patchy and nodular process, distorting the vessel and perhaps narrowing or occluding its lumen The essential lesion arises in the intima and consists in deposition of fat, followed by sclerotic changes. These may cause narrowing of the lumen or aneurysmal dilatation and even rupture of the vessel

Arteriosclerosis comprises the changes in the smaller vessels, the arterioles, found in association with hypertension. The response is first spasm and later medial hypertrophy and hyaline change and thickening of the intima of the vessels.

Atherosclerosis occurs in the older age groups, whereas arteriosclerosis or arteriolar sclerosis occurs in younger patients. In the brain this is the same disease as essential hypertension

The softening of the brain which ensues on atherosclerosis of the larger arteries is the result of an occlusion of an artery already narrowed by blood clot, a true thrombosis The softening which ensues on the sclerosis of arterioles is probably the result of intimal changes.

In the presence of either atherosclerosis or arteriosclerosis, if cardiac weakness supervenes in a person who has cerebral arterial disease, serious consequences may result, impeding the cerebral circulation

Hypertensive Encephalopathy (*Cerebral Crises*). Hypertensive encephalopathy may occur in those who have essential hypertension or in those who have glomerulonephritis or other renal ailment accompanied by hypertension.

In *acute hypertension*, attacks of severe headache occur which are followed by vomiting, drowsiness, bradycardia, convulsions and perhaps coma These attacks may be preceded or followed by focal symptoms and signs which clear up without residua. These symptoms are similar to those present in acutely raised intracranial pressure However, mental deterioration may ensue. The patient can recall remote events, but new impressions and concepts are grasped with difficulty and thought processes and comprehension are confused and slowed Emotional instability, crying and laughing excessively are common. If life should be sufficiently prolonged, dementia may ensue

On ophthalmoscopic examination retinal changes indicative of severe hypertension are often present In these patients often there is spasm of the retinal arteries [illegible] result- [illegible] ever, [illegible] ts of when widespread foci of destruction are present, [illegible] the attack may not follow There is frequently present papilledema of a magnitude of several diopters

In *chronic hypertension* of a severe grade in an elderly patient, there may occur headaches and vertigo, transitory amaurosis, hemianopsia, aphasia, monoplegia and hemiplegia, and in some instances fits As soon as the spastic artery or arteries relax and there is a restoration of the lumen so that blood can flow through, the ischemic brain recovers and the paralysis or other disturbance disappears.

The larger arteries of the arm or leg may participate in such spastic episodes

which are manifested by paresthesias and color changes in the involved extremities. In the extremities the pulse is diminished or lost and the extremity is cold.

On examination the larger arteries, for instance, the radial arteries, are hardened, and palpable nodules may be present. When the arm is flexed, the artery appears to be too long for the arm and it pulsates in two planes. Often the pulsations in the dorsalis pedis and posterior tibial arteries are decreased in volume. The blood pressure is characterized by an increased pulse pressure, for instance an average reading is 180 systolic and 70 or 80 diastolic. Retinal atherosclerosis is evidenced by narrow nodular arteries giving a wide light reflex and depression in the veins where the arteries cross them.

The diagnosis is obvious from the foregoing description. However, caution is exercised before atherosclerosis is assigned the main etiologic role in production of the symptoms from which the patient suffers because these patients may have an expanding intracranial lesion which may require time to enable a certain diagnosis to be made.

Apoplexy. Apoplexy is an acute condition caused by hemorrhage, thrombosis or embolism in the brain, and characterized by coma followed by paralysis or death (see Chapter 6)

The physician may not make a definite diagnosis immediately after observing and examining a patient during an apoplectic fit Generally, however, if the patient has severe essential hypertension or is aged, a cerebral vascular disease is the cause of the convulsion.

The differential diagnosis between cerebral hemorrhage, embolism or thrombosis cannot be made with certainty Hemorrhage comes on more suddenly than cerebral embolism or cerebral thrombosis, may be preceded by sudden severe headache, and is associated with more severe general shock and unconsciousness than are present in apoplexy due to other causes. Blood in the cerebrospinal fluid is the only certain criterion of hemorrhage

Some brain tumors give rise to thrombosis of neighboring cerebral vessels and thus lead to diagnostic difficulties. Some cystic gliomas of the cerebral hemispheres *of adults are particularly likely to bleed. The first manifestation of such a tumor may* be an apoplectic seizure which differs in no way from that seen with atherosclerosis. As with a thrombosis due purely to vascular disease, the patient's condition may then improve, but soon extension of the lesion becomes apparent from the spreading manifestations and the developing intracranial hypertension (see p. 338).

Apoplexy Without Focal Findings. Apoplexy without focal findings is commonly observed The patient falls to the ground unconscious, with changes in color, respiration, and coma. Examination during the fit or in the stage of recovery discloses absence of focal symptoms. Following the attack there is usually cerebral dysfunction Succeeding attacks will occur with less fortunate recoveries and with more definite manifestations

Focal Findings Without Apoplexy. Frequently a patient who has atherosclerosis will be found to have focal weakness or palsies of the face or perhaps of a hand Often the muscular palsies, if one half of the face is involved, will be considered to be a Bell's palsy However, in the beginning there may have been also ataxia and difficulty in swallowing, a combination of manifestations obviously not due to a single lesion. These widespread manifestations are due to multiple focal vascular lesions. The diagnosis of focal vascular lesions is supported if the patient has had an angina pectoris or a coronary occlusion.

When widely dispersed cerebral symptoms are present in a patient who has a malignant tumor in the breast or elsewhere in the body, the possible diagnosis of metastatic malignancy of the brain is considered

Pseudobulbar Palsy. Pseudobulbar palsy is commonly caused by atherosclerosis of the cerebral blood vessels with multiple sites of softening Such processes also

may follow syphilitic vascular disease, general paresis, and infections. Ther disorders of speech, swallowing and chewing.

There is a nasal, explosive voice. The pronunciation of consonants is avc The volume of the voice is diminished, often to a whisper. These patient: aphonic but not anarthric. Mastication and deglutition are affected so that accumulates in the cheeks and above the gums. The swallowing is poorly perfo and the patient frequently chokes on food. The face is sad and inexpressive. S taneous laughing and crying are frequent and cannot be voluntarily stopped D ing of saliva is present However, with good nursing care these patients often for many years, and spontaneous improvement is common. Death usually oc from inanition or bronchopneumonia caused by aspiration of food.

Subarachnoid and Subdural Hemorrhage and Hematomas. Most forn cerebral hemorrhage occur in the later years of life or in persons whose cer blood vessels have been damaged by sclerosis, tumors or intercurrent infection. condition commonly called spontaneous subarachnoid hemorrhage, however, pears frequently in youth and in early middle age, often due to congenital malfo tions resulting in aneurysms or in arteriovenous fistulas of the vessels.

Subdural spontaneous nontraumatic hematomas may be manifested as an a cerebrovascular accident or as a slowly expanding intracranial lesion

The differentiation of subdural hematoma and subarachnoid hemorrhag based on the recovery of blood from the subdural space while the spinal fluid is cl When blood-stained fluid is obtained from both punctures, the origin of the blee is obscure The history, however, offers some aid, for subarachnoid hemorrha usually due to rupture of an aneurysm of the circle of Willis. The ventriculog shows normal or dilated ventricles in subarachnoid hemorrhage and compre ventricles in subdural hematomas.

The neurosurgeon may find a subdural hematoma at the time of operation stead of a suspected brain tumor.

Vascular Disorders of the Cerebellum (*Arterial Hemorrhage and Oc sions*) Occlusion of a cerebellar artery usually does not produce symptoms. Beca of the intimate anastomoses of the cortical branches, hemorrhage into the wl matter produces definite symptoms. Sudden death may ensue because blood rupt into the fourth ventricle, or the bulging cerebellar roof of the fourth ventricle r compress the medulla oblongata

If recovery from the stroke occurs there are present the syndromes produced interference with the blood supply of the cerebellum including that of the supe cerebellar artery and the posterior inferior artery (see Chapter 6)

When circulation to the cerebellum is interfered with by occlusion of the *super cerebellar artery*, there is a disturbance of skilled voluntary movements There ipsilateral in-co-ordination of skilled voluntary movements with loss of sense of p and temperature of the opposite half of the face and body. The onset is genera sudden, and there is gradual improvement. A disturbance of postural fixation a muscle tone is permanent.

... result from invol

intention tremor. In addition there is present the cerebellar gait consisting of staggering. The characteristic signs of medullary involvement include ipsilateral lo of corneal reflex and pain and temperature sensation to the face associated wi contralateral pain and temperature loss of the body. Cranial nerve signs inclu vertigo, nystagmus, Horner's syndrome, difficulty in swallowing and hoarsenes The cause is usually thrombosis, and the prognosis is good for satisfactory fun tional recovery.

Air Embolism of the Nervous System. Air embolism occurs as the result of the liberation of nitrogen in the blood stream due to sudden reduction of atmospheric pressure and from the accidental introduction of air or other gases into the vascular system during therapeutic procedures.

The common therapeutic procedures which are known to have caused air embolism to the nervous system are: a large intravenous needle accidentally left open while in a vein, antrum irrigations and injections of air into the pleural cavity.

The patient suddenly collapses and unconsciousness and convulsions usually occur If the patient does not die at once, there are usually fever, cyanosis and dyspnea for some hours. Hemiplegia often is observed. Transient blindness is characteristic evidence of air embolism. Generally improvement begins within 1 or 2 days and full recovery ensues Permanent symptoms of disability may result.

Fat Embolism of the Brain. Fat embolism results from (1) fracture of one or more bones, (2) extensive bruising of fat deposits or (3) surgical operations on obese patients.

Within a few hours to a few days after an injury or a surgical operation, symptoms develop with rapid respiration, rapid, feeble pulse, cough, cyanosis, blood-tinged sputum and fever. Some hours later the emboli pass through the capillaries of the lungs and begin to reach the brain and other organs. The patient becomes restless, delirious, stuporous and finally comatose Convulsions often occur. Focal signs such as strabismus, hemiparesis and localized twitchings may occur. Many petechiae are distributed over the thorax and other parts of the body and in the conjunctivae and mucous membranes. Fat globules may be present in the urine and sputum Death almost always results when the symptoms are severe.

Venous Disorders. In the congenital angiomas which involve the brain the veins as well as the arteries may participate in the anomaly When there is a direct connection between artery and vein, without any intervening capillary bed, there is a rapid flow of blood from a high pressure to a low pressure system and as a result a noise or bruit develops. Such noises and bruits are synchronous with the heart beat.

Venous Angiomas. Venous angiomas are associated with malformations of the brain and occur in the meninges and the cortex and deep in the brain tissue. They may be manifested by focal epilepsy.

The diagnosis of venous angioma of the brain may be suggested by the known presence of the angiomas in other parts of the body when there is a history of focal convulsions beginning early in life and associated with transient or persistent hemiplegia or other focal signs (see p 315).

Telangiectases. The roentgenographic appearance of the calcification of intracranial telangiectases is characteristic Such a calcification most frequently is situated in the region of the occipital lobe of the brain in an individual who has facial nevi, focal convulsions, hemiplegia and mental deficiency. Other members of the family may be similarly affected

THE CONVULSIVE STATES

Epilepsy. The manifestations of epilepsy are generally a combination of sensory, mental and motor disturbances

The abnormal sensory disturbances are characterized by the aura Abnormal sensations may originate in either the superficial or the deep sensory nerves, or the special senses, especially vision, hearing or taste may be affected. Thus the aura may be described by its association with any of these senses

The mental symptoms too are varied The mind is likely to be profoundly af-

are characterized by the epileptic fit. The true major epileptic fit never occurs without loss of consciousness. The loss of consciousness may be transient and manifested only by cessation of motor activities in petit mal or minor epilepsy. The motor activity may respond as the Jackson type of fit, which is transient in nature, but this too, if due to epilepsy, is accompanied with loss of consciousness In the jacksonian fit, if the consciousness is lost, the disturbance has spread to both hemispheres in the course of progressive cerebral involvement When the fit is generalized, there is a widespread disturbance of cerebral functions

Those epilepsies produced by a discoverable disease process are termed *symptomatic*, those not directly due to any demonstrable organic brain disease, reflex irritation or other abnormal somatic conditions, are termed *idiopathic*.

Heredity plays a definite etiologic role in epilepsy. Occasionally a patient is encountered whose mother or father and all the brothers and sisters suffer from epilepsy. Rarely are both parents affected. In other instances neither parent has convulsions nor is there a known family history. No one would encourage two epileptic patients to marry each other. If they should wed, children should not be contemplated The same warnings are given to two persons in whose families there was a high incidence of convulsions However, some physicians are liberal enough in their views to condone the marriage of a person who has had convulsions, but in whom the convulsions are entirely controlled, and who has a negative family history for convulsions. Such a person may enter parenthood provided the marital partner and the partner's family are free from convulsive disorders, and provided there is a reasonable assurance of financial security.

The immediate causes for the epileptic attacks are difficult to evaluate Certain physiologic conditions such as occur during the first year of life, pubescence, pregnancy, and the puerperium are often associated with the first attacks. Psychic disturbances, such as shock, fear, other emotions and mental overwork, seem to precipitate a fit. Illness such as tonsillitis and scarlet fever may be associated with the initial attack. The onset of any of the acute infectious diseases in children may be associated with a generalized convulsion. In most instances such a convulsion must be regarded as a manifestation of the acute infection, for these children will not have convulsions later in life However, the incidence of convulsions in association with acute infections is somewhat higher in those children who are later to suffer from epilepsy than in others Various organic brain diseases, trauma, and disorders referable to the ears, eyes, nose and alimentary tract, when associated with epilepsy, have given rise to the term reflex epilepsy A reflex epilepsy therefore seems to arise from an abnormal sensory impulse originating in a diseased organ Alcohol, in susceptible persons, is a precipitating agent of great significance

The age of onset is difficult to determine, because minor attacks may not be recognized, and a nocturnal occurrence of the major attacks may obscure their recognition, they have been interpreted as nightmares or as being dead asleep—sleep paralysis The first-born seem more likely to be affected than other members of the family.

The course of epilepsy is exceedingly variable The first attack may be major and of severe intensity, and this may be repeated several times within 24 hours Thereafter a certain degree of rhythm may characterize the course of the affection. Frequently the major attacks may occur only at night as the so-called nocturnal epilepsy. Later they may appear during the daytime

Some epileptic patients have a rapid succession of several major attacks in each period of disability. This condition is not status epilepticus, for in status epilepticus a person who has been suffering from major attacks undergoes a succession of severe fits with extremely short intervals between them, becomes profoundly exhausted, and lapses into a stupor or coma with hyperpyrexia. In some cases the status ends in death, probably owing to exhaustion of the cerebral centers or to

cardiac failure. Status epilepticus usually is precipitated by the patient indulging in alcoholic beverages and forgetting medications.

The varied pathologic changes of idiopathic epilepsy are interpreted as a result of trauma sustained during the attacks and not as the cause of epilepsy. If there are any changes present at all in the brain these may be described as an increase of glia of the first and second layers of the cortex The glial fibrillary groundwork is diffusely thickened around the blood vessels The ganglion cells show various stages of ischemic degeneration and, in many places, they completely disappear. Certain regions of acute change, comprising complete or incomplete softenings, are found along the blood vessels. This change in the blood vessels and thus the blood supply of certain portions of the brain is not associated with organic occlusions of the blood vessels. It is likely, therefore, that the vascular disturbances are concomitants of convulsions.

Dilated, abnormally placed ventricles, dilated subarachnoid spaces, subdural hematomas, and cerebral edema have been observed in epileptic brains.

The trauma incurred by the epileptic patient during spells is rarely of a serious nature unless the patient falls from a height, into water, or in the way of a moving vehicle, or strikes the head against an object, giving rise to a subdural hematoma.

The attacks, fits or seizures of epilepsy are classed in three groups: (1) minor seizures or petit mal, (2) more violent seizures, mainly with progressive motor manifestations, the so-called jacksonian type of epilepsy and (3) the major seizures or grand mal Except for the grand mal seizures these groups overlap and often are not distinctive.

Petit Mal (*Minor Epilepsy*). The petit mal or minor attacks are extremely variable in character, and when they occur without major attacks, their relation to epilepsy may not be suspected by the patient. In fact, some seizures of minor epilepsy may be difficult of detection except by the experienced physician. The minor seizures may consist of transient dizziness, faintness, indescribable sensations, dazed states, hot flushes, pallor, vomiting, belching, or temper tantrums The minor attack leaves no memory that loss of consciousness has occurred. Suddenly the musculature is relaxed and what is being held in the hand is dropped, or there is a cessation of conversation for a moment and then speech is resumed by continuing with the conversation If a complete loss of consciousness does not occur, the patient may be aware of the occurrence of a spell When some consciousness persists, only the patient may be aware of the spell

Minor attacks may take the form of sudden sensory phenomena related to the visual, auditory, or gustatory sensations. There may be peculiar rushing sensations through the body or sudden jerks and starts The minor spells sometimes take the *form of an aura, which precedes the usual major attacks, as if the attack were* incomplete

Grand Mal (*Major Epilepsy*). Prodromal symptoms usually precede the major attacks [illegible]
may con[illegible]
of giddi[illegible]
one or all extremities. Sudden but transient abdominal pain, feelings of oppression or choking, and hiccough or pounding of the heart are common prodromes. Prickly sensations or numbness may appear in an extremity or up the back.

During a day or two preceding an attack the patient may be irritable, lethargic, or euphoric, or may have feelings of impending disaster.

The *aura* commonly arises in the epigastrium, but frequently it appears in an extremity, and auras do arise in any part of the body or viscera.

Auras may be situated in an arm or a leg or in one side of the face as sensations of numbness, tingling or pain. Frequently, one half of the tongue tingles, and the jaw may deviate or the face may be drawn to one side. Spasm and twitching of an arm associated with numbness, tingling, or a sensation of pins and needles may precede the attack. Muscular movements may involve the arm, the head, the trunk

are characterized by the epileptic fit. The true major epileptic fit never occurs without loss of consciousness The loss of consciousness may be transient and manifested only by cessation of motor activities in petit mal or minor epilepsy. The motor activity may respond as the Jackson type of fit, which is transient in nature, but this too, if due to epilepsy, is accompanied with loss of consciousness. In the jacksonian fit, if the consciousness is lost, the disturbance has spread to both hemispheres in the course of progressive cerebral involvement. When the fit is generalized, there is a widespread disturbance of cerebral functions

Those epilepsies produced by a discoverable disease process are termed *symptomatic*, those not directly due to any demonstrable organic brain disease, reflex irritation or other abnormal somatic conditions, are termed *idiopathic*.

Heredity plays a definite etiologic role in epilepsy Occasionally a patient is encountered whose mother or father and all the brothers and sisters suffer from epilepsy. Rarely are both parents affected. In other instances neither parent has convulsions nor is there a known family history. No one would encourage two epileptic patients to marry each other. If they should wed, children should not be contemplated The same warnings are given to two persons in whose families there was a high incidence of convulsions. However, some physicians are liberal enough in their views to condone the marriage of a person who has had convulsions, but in whom the convulsions are entirely controlled, and who has a negative family history for convulsions Such a person may enter parenthood provided the marital partner and the partner's family are free from convulsive disorders, and provided there is a reasonable assurance of financial security

The immediate causes for the epileptic attacks are difficult to evaluate Certain physiologic conditions such as occur during the first year of life, pubescence, pregnancy, and the puerperium are often associated with the first attacks. Psychic disturbances, such as shock, fear, other emotions and mental overwork, seem to precipitate a fit Illness such as tonsillitis and scarlet fever may be associated with the initial attack The onset of any of the acute infectious diseases in children may be associated with a generalized convulsion In most instances such a convulsion must be regarded as a manifestation of the acute infection, for these children will not have convulsions later in life. However, the incidence of convulsions in association with acute infections is somewhat higher in those children who are later to suffer from epilepsy than in others Various organic brain diseases, trauma, and disorders referable to the ears, eyes, nose and alimentary tract, when associated with epilepsy, have given rise to the term reflex epilepsy A reflex epilepsy therefore seems to arise from an abnormal sensory impulse originating in a diseased organ. Alcohol, in susceptible persons, is a precipitating agent of great significance

The age of onset is difficult to determine, because minor attacks may not be recognized, and a nocturnal occurrence of the major attacks may obscure their recognition, they have been interpreted as nightmares or as being dead asleep—sleep paralysis The first-born seem more likely to be affected than other members of the family.

The course of epilepsy is exceedingly variable The first attack may be major and of severe intensity, and this may be repeated several times within 24 hours. Thereafter a certain degree of rhythm may characterize the course of the affection Frequently the major attacks may occur only at night as the so-called nocturnal epilepsy. Later they may appear during the daytime

Some epileptic patients have a rapid succession of several major attacks in each period of disability. This condition is not status epilepticus, for in status epilepticus a person who has been suffering from major attacks undergoes a succession of severe fits with extremely short intervals between them, becomes profoundly exhausted, and lapses into a stupor or coma with hyperpyrexia. In some cases the status ends in death, probably owing to exhaustion of the cerebral centers or to

automatism occurs The patient wanders away, talking when necessary, but completely amnesic for his normal personality. Many of these psychomotor attacks have much in common with the dreamy states which occur with lesions of the temporal lobes.

Status epilepticus is a serious condition in which the patient has one generalized convulsion after another in rapid succession. Usually consciousness is not recovered between attacks. Death may result. Status epilepticus may occur in an epileptic person when therapy is improper or inadequate or when satisfactory medical management is suddenly discontinued, often during an alcoholic bout. However, status epilepticus may occur in those who have never had any treatment.

EXAMINATION IN EPILEPSY During the major attacks, the pupils are usually dilated and rarely react to light The reflexes, including the corneal, are usually abolished Changes in respiration and increase in pulse rate and blood pressure may precede changes in muscular tone and thus suggest a medullary origin of the fits.

After a severe generalized fit deep reflexes may be absent and an extensor plantar response present for some hours; the patient may be unable to understand spoken words, temporary bilateral facial weakness and irregular coarse ocular nystagmus may be present for some time after the seizure.

Injury may be present which was incurred by the physical impact of the limbs, injury of the blood vessels may occur Corneal and subcutaneous hemorrhages appear frequently

In the chronic epileptic patient, owing to vascular lesions which are the results of the fits, there may be present a modification of tonus resembling an extrapyramidal type of rigidity and posture. Other neurologic signs may be those of a slowly progressive, bilateral degeneration of the pyramidal system or a progressive pseudobulbar palsy with contractions in flexor attitudes. Neurologic signs are rare in all except those who have severe forms of the disease.

During the period between attacks a leukopenia and a relative eosinophilia may be present Immediately after an attack often there is leukocytosis associated with a rise in temperature During the attack the blood pressure and the cerebrospinal fluid pressure are increased. Frequent casts and variable quantities of albumin occur in the urine after an attack.

Electro-encephalograms of patients who have epilepsy, and of their relatives, often reveal cerebral dysrhythmias all of the same type The cerebral dysrhythmia seems therefore to be inherited and constitutional It can be demonstrated in twins and nonepileptic persons in the same family However, cerebral dysrhythmias are not synonymous with epilepsy Many apparently normal persons have some abnormality in their electro-encephalogram The full significance of these facts has yet to be determined

DIAGNOSIS OF EPILEPSY The most difficult part of the diagnosis in epilepsy is the separation of symptomatic from idiopathic forms of the disease. Numerous conditions of an organic nature, especially brain tumors, are associated with epileptiform fits

The convulsive seizures themselves are to be differentiated from hysteria and malingering. The hysterical fit does not show the progression of tonicity, there is not the deep unconsciousness, and the convulsions are not orderly. There is a peculiar grotesque excitability during which the patient is never completely unconscious The convulsions usually occur after some emotional disturbance, and lack the periodicity of the epileptic, and finally, the hysterical personality is present. The spells usually occur in the presence of other persons, and the patient rarely injures himself

The malingerer has usually an obvious cause for his procedures and performs his convulsions in front of people, never alone. He rarely hurts himself when

or the leg before loss of consciousness. Twitching of the thumb and index finger, and movements of the same side of the face often appear simultaneously. Bilateral and generalized auras are but increased distributions of the numbness, tingling, or pains and twitching, jerking in the limbs, and tremor of the localized auras. However, shivering and faintness are truly generalized auras.

Auras involving the special senses may be manifested by gustatory or olfactory sensations and smacking of the lips. Such auras are comparable to those which accompany uncinate fits. Visual auras consisting of flashes of light, of color, and of hallucinations of movement may appear Auditory auras of hissing, ringing and other noises are frequent

Major attacks of epilepsy often commence with a wild, harsh, screaming sound produced by expelling or sucking air through the glottis. The cry occurs at the time of loss of consciousness.

The first part of the convulsion is a tonic muscular spasm. The head and eyes may be rotated to one side The facial muscles are in strong contraction, the fingers flexed at the metacarpophalangeal joints and extended at the others. The thumb is adducted into the palm, the elbow joint is flexed to about a right angle. The legs are extended and the feet inverted. The muscular contractions are bilaterally equal. Respiratory movements are arrested until deep cyanosis and engorgement ensue. Occasionally, the tonic spasm may be so violent that a shoulder, hip or mandible may be dislocated. Sometimes fractures of bones occur, including fractures of the jaw and compression fractures of the vertebrae.

When the patient is almost asphyxiated, the tonic muscular spasm changes to a clonic one As the remissions become greater, the contractions become stronger. Finally, as the remissions become longer, the spasms cease.

Saliva mixed with air bubbles is spit and spattered from the mouth by the *forcible clonic movements causing the so-called foaming at the mouth* The patient frequently bites the tongue or the cheek. A tooth may be dislodged. Loss of control of the urinary and anal sphincters and the involuntary passage of urine and feces is common and diagnostically suggestive

The convulsion may consist only of loss of consciousness and tonic spasm end*ing without the appearance of clonic intermissions.* These sudden collapses and loss of consciousness resemble a benign syncope of circulatory origin

After an attack the patient may pass directly into a heavy sleep, often lasting for hours, or he may awaken from unconsciousness for a brief period and then lapse into a deep sleep. The days immediately following an attack are associated with generalized muscular soreness, lethargy, and hebetude. There may be a persistent weakness in an arm or a leg for a few days after the attack. If such weakness does not recede within a few days, a brain tumor is suspected.

A type of major attack, the *cerebellar fit,* begins with stiffening of the entire musculature. The patient becomes rigid in extension, the back is arched and the head extended in opisthotonos Extreme cyanosis occurs as a result of rigidity of the thoracic musculature Gradually, with relaxation, the apnea gives way to shallow irregular respiration; then respiration becomes normal and consciousness returns. These attacks are often followed by changes in the sensorium.

In an *akinetic fit* the patient falls unconscious without an aura Consciousness is quickly recovered The upright posture is maintained without subsequent disability.

A rare type of attack is the so-called *inhibitory epilepsy*. Instead of a local motor seizure, a transient focal paralysis occurs [illegible] temporary

Epilepsy consisting of periods of depression or derangement attain the s[illegible] homicidal. There are spells in which a peculiar [illegible]

and by transient periods of muscular weakness. Either characteristic may be produced by sudden emotional stimuli, of which amusement with laughter is the one most commonly operative

Unless the physician is cognizant of this syndrome and if it is not clearly described by the patient, it is likely to be interpreted as an epileptic seizure. In the accesses of cataplexy, there is no diminution of consciousness. When present, these symptoms are of daily occurrence

The Fainting Attack (Vasovagal Syncope). The faint is a characteristic manifestation of sudden and transient cerebral anemia, and though most frequently seen in the child or the adolescent, it may occur in the adult also. The factors which give rise to it are the fasting state, fatigue, unpleasant emotions, the debility that may follow illness, and confinement in a hot and ill-ventilated room. In weakly subjects the sudden assumption of the erect posture may suffice to induce a faint. A faint rarely occurs when the subject is leaning forward or is lying down. The fall in blood pressure and the attendant loss of consciousness indicate splanchnic dilatation from vasomotor failure (see Chapter 5)

The family and the patient may dismiss a minor or a major attack of epilepsy as a faint The physician is careful not to sanction such a home-made diagnosis until he can be sure about it, lest he become involved in the mistake In epilepsy there is no slowing, weakening or irregularity of the pulse.

In the majority of instances the circumstances leading to the attack and the general emotional status of the patient render diagnosis simple In the faint there is no tongue-biting or loss of urine or feces during the attack

The Faint and the Valsalva Maneuver. In the "mess trick" (played in a mess or at a party) the uninformed person is persuaded to hyperventilate for about a minute and then his chest is suddenly compressed by someone standing behind him He usually loses consciousness for a few seconds. The hyperventilation leads to dilatation of blood vessels of the muscles and constriction of blood vessels of the brain. Compression of the chest causes the victim to perform an involuntary Valsalva maneuver, which in the presence of peripheral dilatation is sufficient to reduce effective blood pressure and consequently cerebral blood flow to levels that cause unconsciousness

In the "fainting lark" the uninformed person squats and takes 20 deep breaths, then rises quickly to his feet, closes his nostrils with his fingers and blows hard. He then drops to the ground and "passes out" for a period of about half a minute. The mechanism in the fainting lark is essentially the same as in the mess trick, except that a voluntary Valsalva maneuver replaces the involuntary response to chest compression with the added factor of the fall in blood pressure produced by rising from the squatting posture.

COMMENTS ON CONVULSIVE DISORDERS

The commonest of convulsive disorders is the epileptic fit The epileptic fit affects but few of the general population and it is largely confined to younger individuals The commonest fit occurring in older persons is of vascular origin, a hemiplegia, monoplegia or paraplegia. Brain tumors are uncommon causes of fits Likewise a fit as a manifestation of neurosyphilis is rare

A sudden convulsive seizure in the presence of gross cerebral symptoms in a patient who has previously enjoyed good health is suggestive of *hemorrhage*, either in a glioma or from an aneurysm, gliomas being, from their loose texture and high vascularity, particularly liable to spontaneous hemorrhages Aneurysms, especially nonsyphilitic congenital aneurysms, run their course at first without symptoms, they are prone to recurrent leakages of blood into the subdural and subarachnoid spaces In the latter event, there is sudden intense headache with rigidity at the back of the neck, Kernig's sign being positive.

allowed to fall. He presents none of the vegetative signs, and can be aroused from his supposed stupor by the production of pain or a dash of cold water in the face. The production of pain or dashing cold water on a patient are both undesirable procedures in the practice of medicine. Of the two procedures it is much more effective to dash cold water on the malingerer's face. A definitely abnormal electroencephalogram practically excludes hysteria as the sole cause of the convulsions. It does not exclude the possible presence and importance of functional emotional disturbances

The biting of the tongue and the loss of sphincteral control are indicative only of a complete loss of consciousness during a fit and have no further diagnostic importance.

In the absence of focal or general neurologic signs, and when the foredescribed conditions are accordingly fulfilled, the diagnosis of major or minor epilepsy may be made If there be doubt, observation for varying periods, with the proper administration of anticonvulsants, may be required before a diagnosis can be made

Idiopathic epilepsy does not present a hopeless outlook. Some of those who have this condition can be completely relieved of their attacks by proper treatment; many of the others can have the frequency and severity of their attacks materially reduced A few who have the disease deteriorate rapidly and require domiciliary care and treatment

Pyknolepsy is a minor or petit mal-like epilepsy which occurs most frequently in girls and young women and in young children Major seizures are not usually associated. The spells consist of some mannerism and an extremely short lapse in consciousness There may be smacking of the lips and twisting of the fingers and occasionally flushing or paleness of the face. Consciousness is lost so suddenly that there is no time for auras The patient does not fall if standing or change posture if in bed After the spell, the patient may resume conversation where it was interrupted. Occasionally urinary incontinence has occurred during an attack. The spells may come with great frequency, occurring 30, 40 or more times per day. Curiously, these attacks often cease at puberty or in girls at the onset of menstruation. The presence of many minor spells, without major attacks, unaffected by medicaments indicates a good prognosis. Usually this type of convulsive disorder (pyknolepsy) ceases spontaneously without physical or mental deterioration Cessation of the attacks, in former days, was observed after the shock of administration of vermifuges such as pumpkin seeds The administration of pumpkin seeds is heroic treatment for either epilepsy or worms.

Jacksonian Epilepsy. Epilepsy without loss of consciousness which spreads from the beginning of involuntary clonic contractions in a hand and successively involves the forearm, arm and shoulder is jacksonian epilepsy. Consciousness may be lost if the second hemisphere is involved These attacks are indicative of irritation of the motor projection system in the brain If this irritation should be from a tumor or an injury, the lesion may be in the motor cortex or below in the frontal, parietal, or peduncular structures.

The Hysterical Fit. In the hysterical fit there is no ordered sequence of events, there is no true loss of consciousness, there are no changes in the reflexes, there is no incontinence or tongue-biting, and the patient (of either sex) does not sustain injuries in falling, nor fall in a dangerous place. The eyes are not passively closed as in true coma, but shut, and the attempt to open them with the finger is usually met with a tightening of the lids The convulsion is not a matter of tonic and clonic stages but of struggling which is aggravated by attemps at restraint The hysterical fit may appear to last for hours, phases of apparent unconscious intermitting with phases of activity.

Narcolepsy. Narcolepsy may resemble minor epilepsy. Narcolepsy is characterized by excessive, uncontrollable drowsiness relieved by a short period of sleep,

characterized by zigzag courses across the visual field to which they are limited Vision is possible only between the scotomas. Such scotomas may occur without a succeeding headache.

The attacks of headache are periodic and have no definite time of the day at which they may begin or end. Mild attacks may be of less than an hour's duration. Many patients find that if they lie down and sleep for a short time or if they even relax completely for an hour or more, the pain will cease. Severe attacks may continue for 2 or 3 days.

The first attack of migraine comes usually during puberty. The attacks may be so mild that they are passed unobserved until later in life. It is the onset of severe migraine headaches in later life, particularly at the time of the menopause, that resembles the beginning of headache due to intracranial hypertension

INTRACRANIAL TUMORS

(Brain Tumors)

Brain tumors arise from the neuroglia of the brain The time of onset and the nature of the symptoms, whether general or focal, usually depend on the expansile characteristic of the tumor. Infiltration of the brain by malignant neuroglia (glioma) may delay either general or focal symptoms until the tumor has infiltrated widely and gives focal symptoms or expands enough to produce the symptoms of intracranial hypertension. The infiltrating anaplastic cells pass between the functional units of the brain and find new places to grow without disturbances of the functional units until they are compressed by an abundant or localized growth of the anaplastic cells There is no definite relationship between the size of the tumor and the symptoms which it produces, nor between the symptoms and the amount of invasion of the brain which may be present The relationship lies in the localized growth of the cells in or near the vital centers and to the circulatory disturbances it can produce.

The expansion of the lesion causes an expulsion of cerebrospinal fluid from the cranial cavity. This fluid passes into the venous blood The total volume of the veins is great and rarely is there obvious venous congestion In some cases, however, transient cyanosis, facial edema and sometimes slight generalized edema may be present Facial edema is the commonest of these manifestations. During the periods of rapid increases in intracranial tension the arterial tension may be slightly increased (160 to 170 mm. of mercury). Except for these transient increases the arterial tension remains normal

Venous congestion leads to an increased secretion of cerebrospinal fluid from the choroid plexuses, and to a diminished reabsorption of this fluid into the dural venous sinuses. The volume of cerebrospinal fluid therefore begins to rise, and since the cranial and spinal dural sac is relatively fixed in volume, pressure within it rises. This leads to still further venous compression and thus a vicious cycle is established However, during the course of establishment of the vicious cycle or soon thereafter the outflow of cerebrospinal fluid from the ventricular system may be obstructed The ventricles then distend, compressing the surrounding portions of the brain.

There are four types of cells contained in the supporting structures in the normal brain and spinal cord. astrocytes, ependymal cells, oligodendroglial cells and nerve cells All of these cells may originate malignant tumors. Of these four types of cells the astrocyte is most prone to form a malignant tumor Less frequently do ependymal cells, and still less frequently do oligodendroglial cells, and rarely do nerve cells form neoplasms The general term used to designate the malignant tumors arising from these cells of the supporting structures (the neurogliocytes) is glioma.

Gliomas. A glioma is a malignant tumor composed of tissue (as noted in the immediately foregoing discussion) which represents neuroglia in any one of its stages

Unruptured *aneurysm* of the intracranial portion of the internal carotid artery produces a characteristic sphenoidal fissure syndrome, comprising unilateral ocular palsy, supra-orbital pain, retinal hyperemia and even chemosis. Sometimes the adjacent optic foramen is affected, causing unilateral visual impairment and optic atrophy. If, in addition to the foregoing, there is roentgenologic evidence of erosion of the sella turcica on the side of the lesion, with or without linear streaks of calcification in the aneurysmal wall, supplemented by filling the aneurysm with thorotrast, the diagnosis is complete

A convulsive seizure occurring in a middle aged adult who has enjoyed good health prior to and after the fit requires a differentiation among epilepsy, neurosyphilis and intracranial hemorrhage, tumor or aneurysm.

MIGRAINE

Migraine is a periodic, recurrent, headache which affects several members of a family. It is due to some inherited constitutional defect. The disorder has in common with epilepsy and some headaches due to brain tumor sensory and motor phenomena. The sensory phenomena consist of visual and psychic disturbances *which precede or accompany the cephalalgia.*

Psychic disturbances such as a subjective feeling of difficulty in thinking, of inability to find the proper word, and a consciousness of slowing of all mental processes are commonly present in migraine but not etiologic. Numbness and thickness of the lips and tongue occur in association with difficulty in speech States of confusion, of excitement and of delirium are described which accompany or replace the headaches.

Owing to variations in manifestations, different types of migraine have been described. Most attacks of true migraine are preceded by visual disturbances, but when such disturbance is a special definite feature, amblyopia, the headache is termed ophthalmic migraine. When the attack is followed by ophthalmoplegia, it is ophthalmoplegic migraine Some patients have abdominal pain, "abdominal migraine," during each attack of migraine, or the abdominal pain may occur apart from the headache as a migrainous equivalent.

Ophthalmic migraine frequently is accompanied by some degree of nausea when the headache is most severe Often if vomiting follows, a great deal of relief is afforded, although vomiting may be present for several days without relief. The cause of the vomiting is not evident It may be an expression of an intracranial disturbance, perhaps vagal stimulation. Accompanying the nausea and vomiting there may be vertigo and occasionally bradycardia.

The term ophthalmoplegic migraine is applied to certain recurrent unilateral headaches which are associated with transient palsies of the extra-ocular muscles. The palsy disappears within a few days or weeks, but it is said that it may eventually become permanent

The most characteristic type of migraine is the hemicrania which begins over one eye and extends backward over the whole side of the head or begins in the occiput and moves forward. The pain may commence locally but eventually becomes general. It may move from one side to the other. The pain is frequently felt in the eyeballs and spreads downward into the cheek. There may be tenderness of the scalp which persists after the head pain has ceased. Often successive attacks of migraine are images of preceding attacks in regard to the place of origin and the progression of the pain.

Descriptions of the onset of the headache beginning with scintillating scotomas limited in distribution to that of an homonymous hemianopsia, and variations of the visual defect to the point of quadrantanopsia, can be given by many patients The margins or the whole of some scotomas are described as *resembling* strips of tinsel in a gleaming light being blown by the wind. The visual disturbances are

It was intimated in the introductory paragraphs on brain tumors that the symptoms of brain tumor arise from an expansion of the tumor. An expanding mass in a closed rigid container like the skull will give rise to two kinds of symptoms, namely, general symptoms, from the increased intracranial pressure, and local symptoms, referable to the seat or origin of the tumor.

General Symptoms of Brain Tumors. The general symptoms are characterized by a progressive change in cerebral function without a febrile illness or evidence of vascular disease at the beginning of the symptoms, nor is fever a part of the illness thereafter. If fever has not been present and if there are no evidences of vascular hypertension, for instance, the so-called malignant hypertension of Keith and Wagener, or encephalitis arising during the course of chronic lead poisoning, and the patient is an adult without evidence of hydrocephalus, the presence of headache, papilledema and vomiting is positive evidence of increased intracranial pressure, caused by an expanding lesion of the brain.

MENTAL CHANGE Early in the course of an expanding lesion of the brain, mental changes are present but they are likely to be difficult if not impossible to interpret. In all instances of increased tension within the skull a gradual blunting of alertness, of memory, and of power of attention develops. Episodic irresponsible moods, tantrums of temper, and poor judgment are common

HEADACHE. Headache is a common symptom of increased intracranial pressure. The origin of the headache is regarded by some as being due to stretching of the dural partitions and by others as being due to abnormal tension in the walls of the cerebral blood vessels However, a general rise of intracranial tension may develop without there being a headache. It is well known too that a headache may be produced or increased by a lumbar puncture which lowers intraspinal and intracranial pressure (see Complaint, Chapter 2).

The evaluation of the symptom of headache is difficult since headache is among the commonest of all subjective symptoms Most headaches result from fatigue or have as a basic etiology a psychoneurosis. Migraine headaches may present many features which resemble headache due to intracranial lesions.

The headache of the psychoneurotic is continuous with slight variations over weeks, months, or even years Despite the descriptions of the severity of the headache by the psychoneurotic, cross-examination without comment usually reveals that the complaint of headache is in reality not a cephalalgia at all but sensations of weight, pressure, or constriction in the head. The hysterical patient is pleased to have an opportunity to relate the great suffering that is bestowed by the constant headache The anxious neurotic patient is despondent on being urged to describe the headache However, both the hysteric and the neurotic patients are anxious to convince their friends and the physician of the truthfulness of their suffering.

In contrast to the behavior of the psychoneurotic and the migrainous individual is the behavior of a patient who has a headache of intracranial origin. Such a patient is quietly preoccupied with the cephalalgia. There is economy of movement and of speech Questions or physical examination when the cephalalgia is present are unwanted. The headache is intermittent, not continuous. When the patient is free from pain, the relief is cheerfully admitted During the interval of freedom from pain the patient returns or attempts to return to normal life in the hope and faith of a child that the pain will not recur. Only with recurrence of the headache do these patients become despondent

The headache due to brain tumor is of a sickening throbbing character and it is increased by physical exertion, coughing, sneezing or stooping It has a tendency to develop during the night, awaking the patient in the early morning During its early course the headache often ceases as soon as the patient is awake and has food or drink. Relief may be obtained by propping up in bed In the beginning the pain is intermittent. The paroxysms then become more frequent and more severe,

of development. These stages of development are represented by the progressive development of astrocytes, ependymal cells, oligodendroglial cells and nerve cells. Kernohan and associates have expressed the belief that the term astrocytoma should be used to designate all tumors arising from these cells

Kernohan is of the opinion that there is a clear-cut correlation between the grade of malignancy, the life history of each tumor (the astrocytoma) and the postoperative survival period. The grade of malignancy of these tumors increases with the age of the patients in whom they grow.

On the basis of anaplasia of each of the four adult types of cells in the central nervous system, with the sole exception of the medulloblastoma, which is in a class by itself, Kernohan has offered a new classification of gliomas. The grade of malignancy is designated as 1, 2, 3 or 4 depending on the degree of anaplasia present Grade 1 of astrocytoma represents a typical slow-growing astrocytoma, grade 2 a more cellular, rapidly growing tumor formerly designated astroblastoma, and grade 3 or 4 the astrocytoma, formerly designated glioblastoma multiforme, with low (grade 3) or high (grade 4) degree of malignancy.

Gliomas of the ependymoma group are likewise classified on the basis of four grades of malignancy

The oligodendrogliomas have not been classified according to different grades of malignancy However, the consensus is that most oligodendrogliomas are very slowly growing gliomas It is also well known that there are some which are highly malignant and rapidly growing and these have been referred to as oligodendroblastomas

Tumors composed exclusively or even predominantly of nerve cells are infrequently found in the central nervous system. The majority of such tumors are a mixture of adult nerve cells and astrocytes or dedifferentiated cells of either or both types. These tumors could be graded 1 to 4 depending on the dominance of the anaplastic cells in the growth, and the term neuro-astrocytoma, grade 1, 2, 3 or 4, could be used. The group of tumors described as spongioneuroblastomas would thus be designated neuro-astrocytomas, grade 2 to 4, depending on the degree of anaplasia present in the tumors

Medulloblastomas usually occur in the midline of the cerebellum of children and occasionally in young adults, and only rarely in other parts of the central nervous system Because of the relatively constant and characteristic structure of this type of glioma no attempt to grade its malignancy has been made

Kernohan's suggested modification of the classification of gliomas is given in Table 15-1

Table 15-1. Suggested Modification of Classification of Gliomas

New	Old with New in Parenthesis
Astrocytoma, grade 1 to 4	Astrocytoma (astrocytoma, grade 1) Astroblastoma (astrocytoma, grade 2) Polar spongioblastoma (obsolete) Glioblastoma multiforme (astrocytoma, grades 3 and 4)
Ependymoma, grade 1 to 4	Ependymoma (ependymoma, grade 1) Ependymoblastoma (ependymoma, grade 2 to 4) Neuro-epithelioma (obsolete) Medullo-epithelioma (ependymoma, grade 4)
Oligodendroglioma, grade 1 to 4	Oligodendroglioma (oligodendroglioma, grade 1) Oligodendroblastoma (oligodendroblastoma, grade 2 to 4)
Neuro-astrocytoma, grade 1 to 4	Neurocytoma Ganglioneuroma (neuro-astrocytoma, grade 1) Gangliocytoma Ganglioglioma Neuroblastoma Spongioneuroblastoma (neuro-astrocytoma, grade 2 to 4) *Glioneuroblastoma* And others
Medulloblastoma	Medulloblastoma

From Adson, A W, and Svien, H J, Brain Tumors Diagnosis and Treatment, Rocky Mountain M J, 45 962, 1948

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In contrast to the behavior of the psychoneurotic and the migrainous individual is the behavior of a patient who has a headache of intracranial origin. Such a patient is quietly preoccupied with the cephalalgia. There is economy of movement and of speech Questions or physical examination when the cephalalgia is present are unwanted The headache is intermittent, not continuous. When the patient is free from pain, the relief is cheerfully admitted During the interval of freedom from pain the patient returns or attempts to return to normal life in the hope and faith of a child that the pain will not recur. Only with recurrence of the headache do these patients become despondent.

The headache due to brain tumor is of a sickening throbbing character and it is increased by physical exertion, coughing, sneezing or stooping. It has a tendency to develop during the night, awaking the patient in the early morning During its early course the headache often ceases as soon as the patient is awake and has food or drink. Relief may be obtained by propping up in bed. In the beginning the pain is intermittent. The paroxysms then become more frequent and more severe,

and are at times accompanied by vomiting, the effort of which intensifies the headache. In great increases of tension within the cranium the paroxysms often are terrifying in their intensity. The patient may hold the hand above the head but is fearful to touch the head lest the presence of the hand further intensify the pain. The intervals of freedom from pain shorten, the sensorium is dulled, the voice weakens, and the patient may pass into coma for several hours at a time but will arouse and be weak but free of pain. When periods of coma supervene, the last part of the downward course is at hand, although the duration may spread over months.

During the progression of the headache there is an added sickness, consisting of apathy, drowsiness, blurring of vision, double vision, and defects in memory and attention. The patient may seem to be profoundly preoccupied.

A patient who has an expanding lesion of the brain may have migraine. If so, during the early course of brain tumor there are no definite differential diagnostic criteria. Migraine has the tendency to increase or decrease periodically in intensity and is often accompanied by vomiting just as is the headache of intracranial hypertension.

Vomiting. Vomiting is not a constant feature of intracranial hypertension. When vomiting is associated with increased intracranial tension, it is of a retching, persistent type. It is, as classically described, projectile in type only when the stomach is full. This sort of vomiting is characterized by not being preceded by nausea. It is prone to occur in the early morning, it may or may not be accompanied by a headache. It is less likely than the headache to be precipitated by exertion or by stooping. Transient unconsciousness may be added to the vomiting and during this occasionally the lips or tongue may be bitten. Terminally the gastric contents may be regurgitated but not vomited, and appear in the nasopharynx as an irritating phlegm causing coughs, choking and respiratory embarrassment, pneumonia and death.

Papilledema. The increased pressure of cerebrospinal fluid within the subarachnoid space is communicated to the fluid within the sheath of the optic nerve. This is recognized ophthalmoscopically as papilledema (see Diseases of the Eye, Chapter 4). Papilledema develops slowly in some and rapidly in others. Papilledema is the most definite diagnostic sign of an expanding intracranial lesion when malignant hypertension is not present. The headaches and papilledema which occur during the course of malignant hypertension may be of the same intensity and appearance as those which occur in an expanding lesion of the brain.

Disturbances of visual acuity or double vision often do not correlate with ophthalmoscopic appearances. Vision may fade gradually, transient blurring occurring during physical exertion, or it may be lost suddenly. If the raised intracranial pressure be not relieved, papilledema proceeds to atrophy of the optic nerve.

Slowing of the Pulse Rate. Slowing of the pulse rate is common in head injuries associated with raised intracranial tension, in some cases of subarachnoid hemorrhage, in abscess and subdural hematoma, and in tumors which cause general signs of raised intracranial tension quickly. In instances of more gradual development, intracranial tension may be greatly increased without any slowing of the pulse, or the pulse rate may fall to 50 or even less, such a fall being of grave import.

Warning. When there are clinical indications of raised intracranial pressure, lumbar puncture or the withdrawal of cerebrospinal fluid should never be performed except for some precise and compelling reason. The fatal issue of lumbar [illegible]

Convulsions. The convulsive seizures of brain tumor [illegible] and indistinguishable from those of idiopathic epilepsy. A convulsion may be the first manifestation, occurring when physical examination of the patient does not [illegible] abnormal physical findings. A convulsion occurring for the first time after

maturity or later requires a consideration of neurosyphilis or brain tumor. These generalized fits have no localizing value, nor do they indicate raised intracranial tension.

Localizing Symptoms of Tumor of the Cerebral Hemispheres. The origin of local symptoms is due to interference with blood supply or to destruction of tissue by the lesion itself If localized pressure from a localized lesion predominates at the outset, the first symptoms may be those of a progressive local lesion of the brain, without signs of a general rise of intracranial tension If the increased pressure is generalized, as often occurs in an infiltrating lesion, the symptomatology is wholly that of intracranial tension and there may be no clue to the situation of the original expanding lesion The absence of early clinical manifestations in many of those who have intracranial tumor depends largely on the plausible explanation that at first malignant cells may be dispersed between the axons and dendrites in a way which will not interfere with their function, and thus there is at least a reasonable cause for the absence of localizing symptoms and signs in the early clinical stages of highly malignant gliomas.

MOTOR SYMPTOMS. Tumors or lesions of the *motor cortex* of the frontal lobes produce irritative and paralytic phenomena

The irritative phenomena consist of unilateral convulsions consisting of spasmodic deviation of the head and eyes to the side opposite from the lesion. These convulsions may occasionally be of the jacksonian type, which commences on the side opposite to the tumor in the face, tongue, arm, or leg, according to the part of the motor cortex which is chiefly implicated In a jacksonian fit the local convulsion, which usually consists of tonic spasm followed by coarse clonic jerks, may be definitely localized to the same group of muscles, or it may spread from them to other groups of muscles, and always in a regular order Jacksonian convulsion differs from ordinary epilepsy in that the patient usually retains consciousness all the time and he may observe the progression of the fit If the convulsion spreads across the middle line, however, and becomes bilateral, consciousness is lost

The paralytic phenomena, in tumors of the motor region, consist in monoplegic weakness of the convulsed muscles during the interparoxysmal periods

A *subcortical growth,* involving the pyramidal fibers, is usually indicated by an initial monoplegia followed later by jacksonian convulsions Convulsions may not be repeated until weeks or months later The deeper the growth, the less tendency is there for the convulsions to localize Tumors of the precentral or motor cortex, if extending across the fissure of Rolando to the postcentral convolution, are usually associated with a sensory aura in the affected limb at the beginning of the motor convulsion

Tumors occurring in the *postfrontal area* may cause unilateral fits with a spasmodic deviation of the head and eyes to the side away from the lesion In left-sided tumors in right-handed patients motor aphasias are common and often persistent. In some left-sided postfrontal tumors aphasia is absent when the individual is right-handed, if the handedness is determinable (see Handedness, Chapter 6).

Tumors on the *orbital surface of the frontal lobe* occurring in the brain or in the meninges may be associated with unilateral diminution of vision, and early and persistent anosmia on the side of the lesion In these there are the same psychic alterations as those which accompany prefrontal lesions.

MENTAL SYMPTOMS Tumors situated on either side of the cortex may or may not give mental symptoms If there are mental symptoms, they appear before the symptoms of intracranial hypertension The mental symptoms consist of alterations in temperament A cheerful person may become depressed and lose power of initiative Yawning and failure of memory ensue Intellectual dullness may be expressed by simple jocularity, together with euphoria and absence of anxiety and concern about the illness. There is a deficiency of attention and often there is a profound

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motor apathy. Late in the course of these lesions defecation and urination may occur during sleep. A motor apathy may be the first symptom of prefrontal tumors.

In instances of astrocytomas, the commonest intracranial tumor of middle-aged persons, the symptoms develop slowly. Weeks or even months pass during which time the patient appears to be and generally is in good physical health. During this time there is a gradual loss of energy and mental alertness In women of the menopausal age the symptoms are those often attributed to the climacteric. There are irritability and apathy If the patient is subject to migraine headaches, these increase in frequency. For a considerable period of time the headache and the vomiting of intracranial hypertension cannot be separated from the same symptoms characteristic of migraine Perhaps the first recognizable symptom characteristic of intracranial hypertension and not characteristic of migraine or the climacteric is drowsiness. The patient sleeps excessively when free from the headache and vomiting

There are those with rapidly growing intracranial tumors who have no detectable change in mental health and no localizing symptoms until the onset of dimness of vision (papilledema) or double vision or a convulsion.

Edema tends to develop around the rapidly growing tumors The edema may cause serious disturbances which end life in a short period of time However, these acute episodes of symptoms are likely to subside, to be repeated several times before death. The immediate cause of death is a rapidly rising fever (temperature 105 to 107 F) and respiratory failure.

On general *examination* of some patients who have frontal lobe tumor there may be no detectable physical or mental aberrations. In others there may be a condition characterized by motor and emotional apathy. In these there may be present an insensibility to what ordinarily rouses feelings of interest, and a hypersensibility to insignificant words or actions There often prevails a dull indifference to the cognitive, conative and affective mental components There may be indifference to, and lack of interest in, pursuits previously vigorously sought and a total disregard of the nature of the illness.

A frontal lobe tumor which exerts pressure backward on the adjacent motor area or pyramidal tract may cause exaggerated tendon jerks with plantar extension in the foot on the side opposite the lesion In lesions of the posterior aspect of the prefrontal region there may be present on stimulation the groping and grasping reflex consisting of a compulsive grasping motion of the fingers or of the toes, on the opposite side from the tumor This reflex occurs only when the patient is psychically confused but not stuporous.

In an occasional patient local cranial tenderness and alteration of percussion note may be present.

Ataxia from a frontal lobe lesion is a unilateral unsteadiness of the foot and leg opposite the lesion, whereas in cerebellar disease the ataxia is in the foot and leg on the same side as the lesion Frontal ataxia may be associated with a tendency to make short backward steps (retropulsion), as if to maintain the stance This aberration of station and gait, if not accompanied by signs of voluntary motor paralysis, on walking may amount to an apraxia of gait

Papilledema, which is late in onset in frontal lobe tumors, tends to be greater on the side of the tumor than on the opposite side, but it is always bilateral. Papilledema on the side of the tumor may result in unilateral optic atrophy However, an optic atrophy may be due to a temporal arteritis or to a retrobulbar neuritis.

Ventriculograms in frontal tumors reveal collapse of the anterior horn of the ventricle on the side of the lesion and if the tumor is large displacement of both anterior horns of the ventricles away from the tumor

Tumors of a *temporal lobe*, situated in the region of the uncinate gyrus, are often attended by convulsive seizures (uncinate fits) commencing with hallucina-

tion of smell or taste, followed by a short period during which there is a feeling of unreality and detachment from the environment The commencement of an uncinate fit may be heralded by noises, such as of bells, heard and vividly described by the patient. An uncinate convulsion usually leaves the feeling that all of the hallucinatory experiences during the fit have been undergone. These beliefs by the patient contrast sharply with the general descriptions of feelings of unreality.

These convulsions may be accompanied by sniffling of the nose, smacking or spitting movements of the lips, and chewing movements of the jaw. In the interim between attacks these patients may complain of feeling as though there were cotton on the tongue and lips. Hemianoptic visual hallucinations are projected to the blind half of the visual fields, which is away from the lesion. These visual hallucinations are complex, elaborate and systematized in contrast to the unorganized scotomas present in lesions of the occipital lobes.

A tumor situated in the *posterolateral part of the temporal lobe* is localized by the ophthalmologist He will observe incomplete visual defects in the contralateral *halves of the visual fields, and as the lesion progresses, he will report that the* hemianopsia has become complete.

Tumors situated in the *postcentral gyrus of the temporal lobe* cause sensory aura and if they extend forward by invasion or by pressure, cause motor symptoms in the corresponding parts which have sensory affections Convulsions are common, they commence with a sensory aura of tingling or of pain, which is present in a lateral half of the face, arm or leg on the opposite side from the tumor. If motor symptoms are present, they consist of muscular spasms. Astereognosis in the hand on the opposite side from the lesion may be present. Anesthesia, monoplegic or hemiplegic, may develop.

If the tumor is *situated on the left side* and the angular gyrus is injured, word blindness occurs which is transient at first but later permanent

If the tumor is situated in or extends deep into the *supramarginal and angular convolutions,* the optic radiations are eventually destroyed Hemianopsia in both visual fields, often attended with hemianesthesia and hemianalgesia on the side opposite to the lesion, ensue

Visual disturbances are significant manifestations of tumors of the occipital region of the hemispheres Tumors in the occipital region produce half-blindness on the opposite side from the lesion

is affected Central vision usually escapes

Tumors of the occipital lobes situated near the cerebellum may extend downward to the cerebellum, and thus cerebellar manifestations may be the presenting symptoms

Large tumors situated deep within the cerebral hemisphere cannot be localized symptomatically

Tumors of the Thalamus. Tumors may be situated in the *thalamus* without producing any definite focal symptoms Involvement of the thalamus produces a degree of hemianesthesia; involvement of the striatopallidal nuclei gives rise to parkinsonian syndrome, on the side opposite to the lesion, accompanied by hemianopsia

Affections of the optic thalamus may cause subjective sensations of pain, heat, and cold on the side of the body opposite to the lesion Often a thalamic tumor fails to give any sensory impairment.

Tumors of the thalamus and corpus striatum may be difficult or impossible to distinguish from chronic epidemic encephalitis. Encephalograms are essential in diagnosis.

Tumors of the Corpus Callosum. Tumors in the anterior part of the *corpus callosum* usually cause mental confusion, deficient memory and attention, and emotional excitability These symptoms are similar to those arising from late neurosyphilis and tumors of the frontal lobes of the hemispheres. Ventriculograms are essential to the diagnosis of a growth involving the corpus callosum.

Tumors of the Corpora Quadrigemina. Tumors in the corpora quadrigemina regions are localized by the presence of a combination of bilateral ptosis with weakness of vertical movements of both eyes and of convergence. The pupils may be dilated and excentric, with loss of the light reflex. *Bilateral deafness, without* vestibular disorder, may result from implication of the posterior corpora quadrigemina Affection of the superior cerebellar peduncle causes cerebellar asynergia simulating a cerebellar tumor

Tumors of the Cerebellum. Tumors of the cerebellum are the commonest tumors of the brain.

The commonest tumors of the cerebellum are the astrocytoma, which is a slow-growing glioma, and the medulloblastoma, which is extremely malignant and which often extends into the meninges In children the commonest tumor of the cerebellum is the medulloblastoma

Extracerebellar tumors which produce pressure symptoms on the cerebellum are commonly situated in the cerebellopontine angle of the posterior fossa of the skull. These tumors may arise from the meninges over the cerebellum (*meningiomas*) or from the sheaths of the cranial nerves, notably the auditory nerve. Tumors of the sheath of the auditory nerve are fibroblastomas, which may be either benign or malignant.

When a tumor or degenerative cerebellar disease is situated in the *anterior lobe* of the cerebellum, the postural reflexes and walking synergies are disturbed. These patients walk with a wide base and stagger or deviate to both sides The gait tends to be stiff-legged owing to exaggerated positive supporting reaction. On occasion it is possible to demonstrate an extensor thrust reflex. If flat pressure is placed against the sole to spread the toes, the leg gives a reflex extensor thrust against the hand

If tumor or degenerative cerebellar disease involves the *posterior cerebellar lobe* there is an interference with the performance of skilled movements, while gait and static equilibrium are maintained. Postural fixation of the extremities is defective, and errors in rate, range, direction and force of voluntary movements occur. On examination, the ipsilateral arm may display hypotonia, which is demonstrated by a tendency for the arm to drift downward and laterally when it is laterally extended Co-ordination tests such as finger-nose and heel-knee show errors in rate, range, direction and force of movements. The movements are slow and jerky, deviate from a direct line, are irregular in force and tend to overreach or underreach the mark

When the *dentate nucleus* also is involved by tumor, combined sclerosis, chronic encephalitis or atrophy, tremor is added to the abnormalities of movements. On walking, the ipsilateral arm lacks the associated swing with the arm contralateral to the tumor There is a tendency to deviate toward the side of the lesion. There is coarse nystagmus on looking toward the lesion, and fine nystagmus on looking away from the lesion The head may be rotated either toward or away from the lesion. On the affected side the tendon reflexes tend to be hypoactive and the knee jerks pendular.

When both of the *posterior lobes* of the cerebellum are involved, there are bilaterally disturbed skilled voluntary movements. Because of bilateral involvement, the gait is more severely involved and dysarthria tends to be severe.

If the tumor is situated in the *cerebellopontile angle* the cerebellar signs develop early, probably owing to pressure on one posterior lobe and the dentate nucleus. There is varying involvement of the eighth, seventh, sixth, fifth, ninth and tenth

cranial nerves as well as brain-stem structures In addition to the cerebellar signs, including nystagmus, there are tinnitus, deafness and loss of labyrinthine function. Diminished corneal reflex and hyperesthesia of the face appear next As the tumor enlarges, facial paralysis followed by paresis of the external rectus muscle of the eye occurs Difficulty in swallowing, hoarseness, hiccough, vomiting and headache are late occurrences

Diagnosis of tumor of the cerebellum or of the cerebellopontile angle is based largely on the presence of a progressive cerebellar ataxia.

Papilledema or other signs of increased intracranial pressure usually are present, and there may be evidence of involvement of the cranial nerves in the posterior fossa or of pressure on the brain stem Vomiting is often the first sign of such lesions and may recur from time to time over a period of months before other symptoms develop

In children a slowly progressive cerebellar ataxia is observed in association with a tuberculoma or with tuberculous meningitis The examination of the cerebrospinal fluid obtained by lumbar puncture, if there is no evidence of increased intracranial pressure, reveals in tuberculous meningitis a lymphocytosis, a diminished concentration of chlorides (normal values 625 to 720 mg. per 100 ml in children and 720 to 760 mg. per 100 ml in adults) and of glucose (fasting normal values in children 70 to 90 mg per 100 ml., in adults 40 to 70 mg per 100 ml.). Tubercle bacilli may be cultured from the spinal fluid. The spinal fluid is clear in the presence of tumors

There is the possibility of the presence of vascular thrombosis or hemorrhage and disseminated sclerosis which symptomatically may simulate tumors of the cerebellum during their early development.

Some of the juvenile cerebromacular degenerations may give rise to cerebellar ataxia among the first symptoms, although disturbances of vision and mental defect are usually present by the time the ataxia is manifested There are also a number of closely related hereditary ataxias which include the familial type of Friedreich. In Friedreich's ataxia there are three components: cerebellar ataxia, posterior column ataxia and pyramidal tract signs.

Tumors of the Cranial Base. Tumors of the cranial base are often sarcomas and metastatic carcinomas Owing to pressure on the cranial nerves before they leave the skull, the symptoms are those of multiple and often bilateral palsies of the ocular, trigeminal and glossopharyngeal nerves Roentgenographically there are sometimes observed defects in the cranial bones where the tumor has invaded the bone and passed on into the cranium Ventriculograms may reveal upward displacement of the third and fourth ventricles

Intraventricular Neoplasms. Tumors within the ventricles give rise to symptoms of increased intracranial pressure When the tumor is movable within the ventricle, the intracranial pressure is not constantly elevated but varies within wide limits The headache may be relieved by placing the head in certain positions In the same way, stooping, straining, sudden movements and certain positions may cause paroxysmal headaches and vomiting

Tumors of the lateral ventricles, when they force their way into the hemispheres, may cause hemiplegia, hemianesthesia or hemianopsia Such tumors may invade the adjacent structures, producing symptoms characteristic of disease of the hypothalamus and infundibulum, optic thalami and lenticular nuclei and the pineal syndrome

Tumors of the fourth ventricle may cause focal signs early. Vomiting often develops before there is definite papilledema Subsequently signs and symptoms indicative of involvement of the cerebellum and pons appear.

Ependymomas. Ependymomas may occur in the lateral, third or fourth ventricles but seem to be slightly more frequent in the fourth ventricle They may occur too in the central canal of the spinal cord

These tumors grow slowly but there is nothing which differentiates them from any other intraventricular tumor Ependymomas often are encapsulated and if successfully localized, they may be removed.

Papillomas of the Choroid Plexus. There is nothing in the course of symptoms of these tumors to distinguish them from any other intraventricular tumors before operation. Treatment consists of localization by ventriculography and operative removal.

Colloid Cysts of the Third Ventricle. Colloid cysts are found only in the anterior part of the third ventricle, attached to the choroid plexus, and are of rare occurrence. Recurrent and periodic headaches may be precipitated by flexing the neck, by straining or by stooping More serious manifestations are slow feeble pulse and low blood pressure accompanying the headaches In a later stage of the process the patient may become stuporous or even unconscious for short periods. The face may flush during the headaches

Meningiomas. The meningioma arises as a proliferation of the cells of the arachnoid villi It grows slowly, does not invade the brain, and never metastasizes to distant organs It may be associated with Recklinghausen's disease, and several members of a family may be affected

The presence of increased intracranial pressure is often the sole indication of a meningioma. A meningioma occurring over the convex surface of the brain gives minimal signs until it has attained considerable size unless it is situated over some structure, injury of which will give recognizable signs early. For instance, if situated on the floor of the anterior or middle fossa, a meningioma may reveal its presence by the appearance of cranial nerve palsies. A meningioma growing from the ethmoidal plate of the frontal bone will compress one optic nerve, giving rise to progressive failure of vision in one eye and unilateral loss of the sense of smell on the same side A tumor on the floor of the middle fossa will produce diplopia, squint, and ptosis from progressive paralysis of the third, fourth and sixth cranial nerves Increased intracranial pressure develops slowly and is of late occurrence.

The course is usually a slow one. The brain is compressed rather than invaded and thus focal signs are inconspicuous The diagnosis prior to operation is made only when there is cranial change which can be detected on roentgenologic examination.

The *auditory fibroma,* or auditory nerve tumor, is often a part (a form fruste) of a generalized neurofibromatosis (Recklinghausen's disease) A single benign neurofibroma may compress and stretch the eighth nerve and cause tinnitus, deafness and vertigo If the fifth nerve is compressed, there are loss of corneal reflex and numbness of the face Compression of the seventh nerve produces Bell's palsy. This is a slowly growing tumor, and deafness with tinnitus may be the only symptom It rarely gives a rapidly developing intracranial hypertension as do intracerebellar tumors, nor is there a well-developed cerebellar ataxia.

Metastatic Neoplasms of the Brain. Metastatic tumors of the brain, especially carcinomas, are frequent Intracranial lesions which cannot be explained on the basis of one tumor are always suggestive of metastasis

Tumors of the nose, throat, eyes and thyroid gland, malignant melanomas and carcinomas of the stomach, colon and the pancreas are likely to metastasize to the brain However, any blood-borne tumor cell may take up abode inside the brain. Malignant tumors may extend into the subarachnoid spaces and produce signs of meningeal irritation and pleocytosis in the spinal fluid (tumor meningitis). Increased intracranial tension is a late event in the course of metastatic tumors of the brain

Roentgenograms of the skull will often reveal multiple regions of absorption of bone which may be sharply defined or indistinct in appearance.

Ventriculograms may offer some difficulties of interpretation. There may be evidences of only one large tumor or the deposits may be so numerous and so small that the ventricular system is symmetric.

Diagnosis of Brain Tumor. The diagnosis of brain tumor is almost always a difficult one to make and rarely is it made early. The diagnosis depends on (1) a progressive loss of neurologic functions; (2) increase in intracranial tension resulting in headache, papilledema, vomiting and stupor; (3) focalizing symptoms, which may be present and diagnostically helpful, and (4) convulsions, which occur in about one half of all those who have brain tumors, for a long time convulsions may be the only symptom

The ophthalmologist often finds the most conclusive evidence of increased intracranial pressure by observing the presence, and measuring the degree, of papilledema Before the presence of papilledema the ophthalmologist may observe visual field defects which are of precise localizing diagnostic value.

In the final analysis it must be remembered that a vascular disease of the brain, accompanied by arterial hypertension, such as the malignant hypertension of Keith and Wagener, or a vascular disease without excessive hypertension, may present all the subjective symptoms and objective findings of a brain tumor and may not be definitely differentiated in some instances except by ventriculography.

The plain roentgenogram of the skull will reveal destruction of the posterior clinoid processes and evidence of intracranial pressure if the pituitary tumor has been present for some time If a meningioma has invaded the skull and has produced thickening and alteration in texture of the bone in the affected region, this is evident on the roentgenogram A tumor may contain calcareous material which casts a shadow and thus reveals both the presence and the site of the growth In and after middle age the normal pineal gland often contains such material, and if a tumor be present in one cerebral hemisphere, the shadow cast by the pineal gland may be displaced laterally A pituitary adenoma or a stalk tumor may produce enlargement and deformity of the sella turcica

The commonest of all intracranial tumors, the glioma and the secondary carcinoma, very rarely give any indication of their presence in the roentgenogram.

If the ventricles are filled with air, the resulting roentgenograms (ventriculogram, encephalogram) may reveal deformity or displacement of the ventricles and thus indicate the situation of a new growth. These tests are best performed by a surgeon capable and trained to undertake any operation that may prove necessary, in case immediate operation should become necessary from a sudden increase of symptoms which may ensue after the introduction of air into the cranium

An intracranial growth that cannot be removed is fatal The malignant glioma and the secondary carcinoma comprise one half of all intracranial tumors and these are not surgically curable Palliative decompression, as a rule, serves to prolong for weeks or months a life of increasing disability and distress.

Cerebral Angiography Recently Craig and associates reported 100 cerebral angiograms made by them at the Mayo Clinic on 77 patients The dye was injected into the common carotid artery In 31 patients suspected of having brain tumor, 16 lesions were identified by cerebral angiography. In 17 of 36 patients suspected of having subarachnoid hemorrhage, a vascular lesion was demonstrated by angiography. In 6 instances the angiograms did not indicate brain tumor, the presence of which was later verified In 2 instances the angiograms were interpreted as indicating brain tumor, but the diagnosis could not be verified at operation Unsatisfactory angiograms were obtained in 10 per cent of the cases owing to technical difficulties.

Cerebral angiography is a helpful diagnostic aid in the localization of intracranial lesions but carries a certain risk to the patient

Radioactive Diiodofluorescein. In the experience of the neurosurgeons of the Mayo Clinic the use of radioactive diiodofluorescein in the localization of brain tumors is valuable in only one half of total cases In those instances in which the dye can be used, this method of localization has given results which are precise enough to be of use to the surgeon in about 4 of every 5 of the cases This experience seems to closely parallel that of Moore and associates, whose technic of testing was, in the greater part,

adhered to in performing the test. Tumors less than 3 cm. in diameter, unaccompanied by a halo of edematous tissue, were sometimes missed, and tumors of the posterior fossa and parasellar region were difficult to localize by this technic.

THE ELECTRO-ENCEPHALOGRAPH. When the brain cells are injured, waves slower than 18 per second with high voltage are present in the electro-encephalogram. Combinations of slow and fast waves are present in those who have petit mal In certain brain conditions abnormal waves are best elicited during hyperventilation.

The dysrhythmias, abnormally slow delta waves, are present when there is an area of abnormal cortex

The electro-encephalograph is employed as an adjunct diagnostic procedure. The apparatus is rarely available and the electro-encephalograms must be interpreted by experts

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Part Three

The Body as a Whole

16

THE CONSTITUTION

In the preceding parts of this book the regional and systemic diseases have been separately discussed It is now proposed to describe some normal and some abnormal conditions which demand consideration of the biology of the individual (body as a whole). In the past, diseases of this nature have been termed constitutional diseases. A constitutional disease may be due to inherent imperfections in the constitution or it may arise secondarily from the progress of regional or systemic diseases.

The constitution of an individual comprises the inheritable, invisible structural components These were formerly adequately described as disposition, diathesis, dyscrasias, character, constitution and individuality Some of these terms may still have descriptive value In a broad sense these structural components were present in the primordial protoplasm of mankind or have been added by the progenitors of man and by man himself during the hundreds of millions of years which have been spent in attaining his present constitution.

The constitution of an individual is individual to himself though subject to constant change by environmental influences and experiences from the time of maturation and fertilization of the ovum

Constitutional stamina is manifest in the morphologic and functional characteristics, external form, performance capacity and resistance to, and in the mode of reaction to, pathogenic influences.

There is an intellectual heritage of all animals at least from the fowl onward by which they recognize those that are sick or injured and avoid or often attempt to destroy them. In man the sorting of the sick individuals from the healthy ones and of the healthy ones of varying capabilities one from another requires extensive information and skill In practice the information on any one individual never can be complete and therefore great caution is exercised and the critical sense is employed to the utmost before arriving at decisions concerning how much of the disability is at the time of study dependent upon a person's constitution and how much is dependent on the immediate externalities. Healthy individuals have their dispositional or premorbid individuality which is so varied that a feeling of well-being and physical capability to one may seem to be a state of incapacity to another Moreover these variables are carried by the individual from health into disease and these may cause great difficulty in the separation of a healthy constitution from a sick one

EXTERNAL CONSTITUTIONAL DIFFERENCES

There are, as is well known, both visible and invisible characteristics of men, women and children. These characteristics form the bases for separation into racial stocks Within a racial stock are races separable by certain methods employed by the physical anthropologist. These methods include descriptions and classifications of color of skin, of hair on head and body, eyes, form of internal eye folds, form of noses and a number of anthropometric measurements. Given a race, within it

will occur certain numbers of individuals who have similar morphologic and physiologic characteristics which set them apart from others in types.

It is realized that millennia have been required to evince the changes in anatomic structures observed in different races of men living in different parts of the world. These changes, in part, may be related to climate, environment, health and food

Climate, Environment and Health (Geomedicine). Genera, species, or races may arise as the result of alteration of function in response to climate and environment These alterations in function may require a change in somatic type.

Coon seems to believe that the peoples of the Mediterranean littoral and the Middle Eastern mountains from Palestine to Northern India and particularly those who live in the moist heat of the forests in these regions probably have deviated less from the original human habitus than any others.

ALTITUDE. Coon believes that the peoples who migrated from the Mediterranean littoral or from Palestine and southern India to inhabit the mountain zone to the north were the first to reveal the evolutionary influence which results from habitation in higher altitudes The influence of altitude is manifested in the increase in size of the thorax and in the surefootedness which are characteristic of the Alpines. The physician is not aware of the work and thought which the anthropologist has expended in order to arrive at these conclusions In clinical diagnosis and in prognosis of pulmonary infections such as tuberculosis the physician is aware that the size and shape of lungs may be related to selection and survival Tuberculosis, for instance, is more disastrous in persons who have long lungs in long narrow chests than in those who have shorter lungs in shorter broader chests.

HEAT AND COLD In contrast to the evolution of big chests and compact bodies as the result of higher altitudes Coon calls attention to the evolution of broad flat chests and gaunt bodies of inhabitants of the hot desert countries The gaunt, flat-chested desert folk have long arms and legs, short, shallow bodies, and narrow hands and feet Their surface area is great in proportion to their volume and weight, thus permitting optimal cooling through radiation and evaporation

In the course of migration northward the progenitors of the natives around the Arctic Sea underwent various regional influences On arrival in the Arctic Zone they had the thick wide chests gained from living at high altitudes, and in time they developed short thick arms, legs, hands, fingers and toes and the thick protective layer of subcutaneous fat that conserves body heat

LIGHT AND CUTANEOUS PIGMENTATION In its effect on the human organism light is more important than heat in maintaining health or in causing disease. Light and heat influence racial variations in the amount of cutaneous pigment and thus color of the skin. However, the skin of the original men in the Middle East was brown Human skin darkens when exposed to ultraviolet light of summer, and it fades to a lighter color in the winter

The principal function of pigment in the skin is to protect the skin and the tissues below it from excesses of ultraviolet light, particularly from the narrow but harmful part of the spectrum. Individual human beings vary greatly in the concentration of cutaneous pigment (melanin) which originates in the germinative layer and moves into the granular layer of the epidermis White peoples have varying quantities of melanin, while the lower layers of the epidermis in Negroes and some Negritoes are packed with it The amount of pigment deposited is inherited, but not as a single factor (see Skin, Chapter 8).

SKIN COLOR AND COLOR AND TYPES OF HAIR Coon postulates that when the ice sheet withdrew to the north over the Baltic States, it withdrew gradually and the great humidity in the warming air filled the skies heavily with clouds. In the Baltic States still the clouds gather by October and remain solidly until April

This phenomenon of fog and darkness affected three parts of the body, the skin, eyes, and hair, of inhabitants of the region The *skin* became blond An extremely

blond skin deviates from the normal or ordinary light brown human skin by having fewer and smaller granules of pigment in the pigmented layers. A person who has a truly blond skin may be incapable of tanning when exposed to wind and sun. The skin becomes red and edematous and, on continued exposure, sloughs. Under the Baltic climatic conditions blondism reached a high level of frequency which has remained high because it has not been disadvantageous there and in the climates where these people have migrated. However, a common skin in a dark cloudy region is pale with little pigment. These pale skins may tan in summer and bleach in winter, and get along without trouble in other environments.

Blond persons usually have blue eyes due to an absence of pigment in the outer layer of the iris (see Eye Color, Chapter 4), and it is the inner pigment shining through the radial and circular muscle tissues that makes the iris look blue.

Two factors at least are involved in *hair color*, melanin, as in the skin and eyes, and a red pigment. The size and number of melanin granules determine hair color, from ash blond to what appears to be black. The lightness or darkness of the hair is due both to the concentration of pigment and to the thickness of the hair shaft. Light hair is not confined to northwestern Europe nor has it ever been.

"Red" hair and brown hair are commonest among the blue-eyed, florid-skinned peoples of northwestern Europe and the British Isles. Ash blond hair is commonest among the pale-skinned, gray-eyed peoples of Central Europe from the Baltic eastward and southward.

Color of the skin, including color of the eyes (see Eyes, Chapter 4) and helical and spiral hair are not recent modifications acquired from environmental influences Helical and spiral hair is the tightly curled hair characteristic of Negroes, Pygmies, and Melanesians, but by no means is it limited to them.

Garn distinguished three basic types of curved hair: (1) *Wavy hair*, which forms a two-dimensional figure. This varies in the linear distance between the crests of the waves. (2) *Helical hair*, which forms a three-dimensional figure. Its loops are of a constant diameter as far as each hair is concerned. These diameters vary individually and racially. Helical hair is usually found among Europeans and European-like populations in other continents, and among Melanesians In Europe the oldest, most marginal population, consisting of the southern Irish, the Welsh, some of the Norwegians and Finns, and the Alpines of Bavaria and adjacent mountain regions, has every kind of hair form, including the helical. (3) *Spiral hair*, which is also three dimensional. The loops diminish in diameter outward from the scalp. In the extreme form of spiral hair the loops are narrow, and intertwine in clusters or rows, leaving patches or swaths of skin bare. This is called peppercorn hair.

Environmental Elements and Food. The elements in the natural environment which stimulate and influence somatic responses and finally racial characteristics are the same ones in which aberrations in the supply may produce health or disease These elements include the various rays from the sun, radiation from outer space as controlled by the angle of incidence of the rays of the sun, by the prevailing presence or the absence of clouds in the sky, the density of the air at different altitudes, and the concentration of solutions of minerals, ingested and assimilated through food and drink These mineral solutions are most important in regard to the size of the individual. For instance, calcium and phosphorus are necessary for bone building, iron is necessary for oxidation in the lungs, iodine for the production of the thyroid hormone, and sodium and chloride are essential for the maintenance and regulation of fluid balance and body temperature The trace elements, manganese, copper, zinc, and cobalt, have necessary and relatively significant functions.

The importance of the innate ability of individual members, or most of them, of a race to live on short rations, and of some to grow fat on short rations, is explained on the basis of selection only. This kind of selection seems to have caused a genetic change in some members in all races so that there are unmeasurable changes in their nutritional requirements. Thus, on the same caloric intake, some are lean while

will occur certain numbers of individuals who have similar morphologic and physiologic characteristics which set them apart from others in types.

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The importance of the innate ability of individual members, or most of them, of [illegible]

[illegible] nutritional requirements. Thus, on the same caloric intake, some are lean while

others are fat. Likewise, because of better nutrition, the well fed are taller than the less favored individuals.

Somatic Types. The range of human physical, physiologic and psychologic normality varies through wide limits The range of normal contours and sizes of the human body is so great that the physician's attention is attracted only when these limits pass beyond the ones he is accustomed to seeing. It is for those reasons that on general physical examination the body size is simply recorded as the height and weight of the individual patient On a more detailed inspection of the patient it is realized that body size depends on a relationship of constants between its component parts

The physical anthropologists have a system of constants for a number of diameters of the body, such as span, shoulder breadth, thoracic breadth and depth, sitting height, pelvic breadth, and the lengths and breadths of the extremities, and many diameters of the head and face These constants and diameters of the body have been employed by Sheldon, Stevens and Tucker, Hooton, and others for the classification of human beings into somatotypes on the basis of their observations of standard photographs in combination with a number of measurements made thereon The classification of various individuals into somatotypes by this method depends on the recognition that human bodies are a composite of the three primary germ layers, namely, (1) the entoderm, (2) the mesoderm and (3) the ectoderm The types of body build in which these components respectively predominate are termed endomorphy, mesomorphy, and ectomorphy

The three components all exist to some degree in every individual, irrespective of race In a human being it is recognized that in toto a blend of the three components is present but that parts of the body may express different qualitative combinations Accordingly, the body is studied in regions the head, face and neck; thoracic trunk, arms, shoulders and hands, abdominal trunk, thighs, calves and feet. The total of these regional assessments gives an average of the entire body

In *endomorphy* emphasis is placed on rounded soft contours The anteroposterior and transverse diameters tend to be equal In mass the abdomen and the thorax predominate over the extremities, the abdomen predominates over the thorax, and the proximal limb segments, over the distal segments. The head is large and spherical. The face is broad, with upper and lower widths equal The neck is short, the limbs are short and tapering, the hands and feet are small The trunk is long, with the thorax wide at its base The maximal transverse diameter of the body is near the iliac crest The skin is soft, smooth and velvety The external genitalia tend to be hypoplastic

In *mesomorphy* emphasis is on the squared, rugged, hard contours The transverse diameter of the body tends to exceed the anteroposterior diameter The mass is concentrated in the trunk, but not unduly so The thorax predominates over the abdomen, the proximal and distal segments tend to be equal in mass The head is variable in size, but muscular ridges are emphasized The face is relatively large and is long, broad, bony and massive The neck is long, length of the limbs is variable, the hands and feet are large and broad, the long trunk has a thorax wide at its apex, the waist is slender and the shoulders are broad The pelvis is sturdy, and the hips are broad. The skin is thick and coarse with large pores The connective tissue is dense, with good turgor. The external genitalia are well developed

In *ectomorphy* the emphasis is on linearity and on fragility and delicacy of the contours The transverse and anteroposterior diameters are small and usually about equal The mass is decentralized, the abdomen is flat and short with a relatively long thorax The limb segments tend to be equal in mass The head is large and long with slight muscle ridges. The face is small, fragile, and tends to be triangular with its apex at the chin The neck is long and slender, the limbs are long, especially in the distal segments, the hands and feet are long and narrow The trunk is narrow and relatively short, and the shoulders are drooping rather than square The skin is thin and dry and has an early tendency to fine wrinkles The connective tissue is thin; turgor is poor. The external genitalia are elongate and relatively hypotrophic.

The data on *somatic body types in children* are incomplete. Any index of body build changes with age; for example, for males Quetelet's index (W/H) is 10 4 at birth, 17.0 at 5 years, 20 8 at 10 years, 30 0 at 15 years; Röhrer's index (W/H) is 2.30 at birth, 1.60 at 5 years, 1.30 at 10 years, 1.38 at 15 years Body build or body type as a morphologic entity is established fairly early. Sheldon and Wetzel agree that it is firmly entrenched by 6 to 8 years of age or possibly earlier There is no doubt that body build is inherited and too is a reflection of the familioracial background

The foregoing somatotyping has so far not proved to be of great value, for the work [illegible] d.

[illegible] based principally on observation, is [illegible] d three main constitutional types and suggested for these types the following descriptive terms, which now are in commonly accepted use: asthenic, athletic, and pyknic; dysplastic applies to mixed constitutional types

The human being of *asthenic type* has a small, short and low head of average breadth The body is narrow but of average length. Subcutaneous fat is lacking, bones are small, and muscles are underdeveloped; slight anemia is characteristic. The chest is flat, the ribs are prominent, and the angles of ribs with sternum are sharp. The weight is very low for the height, and the thoracic circumference is less than the hip circumference The asthenic type is associated with the dysgenital groups, infantilism, feminism and eunuchoidism As an adolescent the asthenic individual grows rapidly without adding bulk Because of slow development of muscles the asthenic individual finds muscular work difficult and has to learn to do it, but when he has achieved muscular development, he can do moderate labor efficiently, although he never becomes muscular in appearance. Senility or the appearance of senility occurs early At from 30 to 40 years of age he begins to lose his hair, the face wrinkles and sinks, and often early in life arcus senilis develops The female of the asthenic type is an accentuation of the male to the point where she not only is asthenic but may be asthenic-hypoplastic

The male of the *athletic type* has a strong skeleton with strong ligaments and muscular support The height is average to tall. The thorax is muscular and well developed, the abdomen is muscular and not protuberant The hips and legs, as compared with the chest and shoulders, seem slender and long. The upper extremities, like the legs, are rather long. All circumferences of the head, neck and thorax are increased by the musculature and the subadjacent bones The bones of the face are prominent and in relief, and the clavicles, wrists, ankles and hands have prominent bone structure The thick skin has good elastic turgor, with relatively little fat in the subcutaneous connective tissue Dysgenic traits, especially traces of eunuchoidism and feminism, may occur. The muscles of the athletic type develop rapidly during adolescence

The female athletic type has a tendency toward masculine facial traits These undesirable features are offset by increase in adipose tissue, giving rounded feminine contours In some of these women there are masculine features of face and body It is the occurrence of the latter that may make the athletic type of woman seem abnormal, the accentuated traits in her are normal for the man.

The *pyknic type* is characterized by average height, broad figure, flabby broad face, and a short thick neck, so short that often the head seems to be placed between the shoulders The abdomen apparently protrudes from the short, deep, arched thorax The extremities are small and rounded with small, fairly well-developed muscles. The hands are small, short and broad, the wrists and the clavicles are small, the shoulders are narrower than in the athletic type, and are rounded and high and appear to approximate the jaw line, owing to the short thick neck The stoutness of the pyknic type is found in the trunk and the protuberant abdomen The abdomen in reality is not excessively fat, as may occur in the asthenic and the athletic types in later life, the fat of the pyknic type is likely to be in the face, hips and calves, forearms, hands and the acromial ends of the shoulders, whereas the legs may remain relatively thin throughout life. In old age, however, the abdominal fat may become greatly increased Both men and women of the pyknic type have excessive amounts of fat in the breasts and about the hips

The criterion for somatic typing, whether it be that employed by the anthropologist or some less precise but clinically more usable method, as advocated by

Kretschmer, will apply to all racial stocks. A somatic type that might be difficult to classify in one racial stock might be well within the limits of normal within another racial stock.

VISCEROPTOSIS. In all of the racial stocks represented in the United States of America there is one somatic type, the visceroptotic, of common occurrence, which has caused much speculation in regard to diseases which have been considered incident to it

An understanding of visceroptosis can be had by reviewing the anatomy of the skeleton in relation to its contained viscera and the normal visceral supports The small centrally situated heart in the long thoracic cage is considered in diseases of the heart The position of abdominal viscera depends normally on peritoneal attachments and on those conditions which influence intra-abdominal pressure. The diaphragm is an important structure in visceral support The efficiency and support of the diaphragm are in turn dependent on a vacuum in the thorax and on the cervical fascia The latter in its continuation through the pericardium is the supporting ligament of the diaphragm A continuation of the support to the abdominal viscera given by the diaphragm is the transversus abdominis muscle In reality, the transversus abdominis muscle is the chief factor in regulating the piston action of the diaphragm

Failure of visceral attachments and the abnormalities in position and mobility due to lack of normal fusion of viscera to the posterior peritoneum may permit ptosis A normal lordosis with the thick psoas muscle forms a shelflike support for the kidneys and narrows the lower portion of the abdominal cavity. Retroperitoneal mesenteric and omental fat assists in keeping the abdominal organs in their normal position. The presence of fat prevents an undue drag upon and stretching of the peritoneal attachments The importance of this fat has been overemphasized in the treatment of ptosis

All of the forementioned anatomic imperfections constitute the *enteroptotic habitus* The enteroptotic habitus is congenital Such factors as faulty posture, childbearing, loss of weight and the presence of large abdominal tumors or recurrent ascites are precipitating factors, they cannot produce visceroptosis except in a person predisposed by a constitutional somatic type which was inherited.

The so-called manifestations of visceroptosis are of psychoneurotic origin. Visceroptosis of constitutionally inadequate persons who live within their physical and nervous capacity is not associated with symptoms.

On examination no clinical importance need be attributed to the discovery of organs in a low position in persons of the habitus asthenicus. The presence of the slouching "fatigue posture" in the visceroptotic person may increase the likelihood of organic dysfunction and production of symptoms

The abdominal wall is examined for evidence of atony and weakness Very often the weak abdominal wall bulges in the flanks when the patient is in the dorsal decubitus position and protrudes excessively in its lowermost portion when the patient is upright Having the patient attempt to raise the head or legs from the examining table while reclining on the back demonstrates the efficiency of the abdominal musculature. The presence or absence of diastasis recti abdominis may likewise be detected in this way In some patients who have acquired ptosis, after bearing children or as the result of large abdominal tumors, diastasis may be extreme.

During the course of the examination of the abdominal wall, visible pulsations occurring synchronously with the heart beat are more prominent in the visceroptotic patient than in the nonvisceroptotic person.

Visible peristalsis may occasionally be observed through the very thin abdominal wall if excessive gas is present in the intestine. In some patients the transverse colon is palpable It is doubtful whether anyone can palpate or observe visible peristalsis

in a markedly dilated descending duodenum in a patient who has extreme duodenal ileus associated with visceroptosis.

The right lobe of the liver may extend to the iliac crest. Because of its free mobility the thin hepatic edge, even though low, may be difficult to palpate. If the liver becomes fixed in a low position it may resemble a tumor. The spleen in visceroptotic subjects is identified by the general contour and mobility and thus is differentiated from splenomegaly. The lower pole of the right kidney is palpable in the majority of patients. In the visceroptotic patient the kidney may be low in the abdomen, or even in the pelvis

The diagnosis of visceroptosis is not difficult The presence of the condition is usually suspected on physical examination and easily confirmed by roentgenologic study. The condition is not mentioned to the patient unless symptoms have been attributed to the visceroptosis by a less informed surgeon or physician

INTERNAL CONSTITUTIONAL DIFFERENCES

Stocks and races have had their origin from human beings living together and interbreeding. Interbreeding is a means of selecting and perpetuating certain arrangements of genes which control everything that an individual is, or that is possible for him to be and to do Inbreeding, despite the fact that each human being has some 44,000 pairs of genes which can be, to a degree, successfully rearranged in the formation of a new individual, may mean the survival or the extinction of these new individuals depending on the resulting constitution and adaptability of them.

Blood Groups. The blood groups O, A, B and AB are genetically separate, and an individual may inherit combinations of two of these genes The group substances which are responsible for the various types of blood are present in the bone marrow, semen, and brain tissues.

In addition to the O, A, and B series, serologists find other group factors which have differential world distribution. One of these is the M-N series An individual can be M, N, or MN These factors cause no agglutination of the blood in transfusions.

There are two major types of the rhesus series, Rh positive and Rh negative (see Erythroblastic Anemia, Chapter 12). It seems that in an inbreeding population either the Rh negative or the Rh positive group may be eliminated

GEOGRAPHIC BLOOD GROUP VARIABILITY IN THE UNITED STATES. In the United States blood group O percentage is increased by 0.32 on the average for each degree southward The most acceptable interpretation is that in the South the hereditary lines of the early settlers, many of whom were Scotch, Irish and Welsh in origin, have been subjected to less admixture from the outside than in the North

From north to south the B percentage averages 0.17 smaller per degree of latitude The A relationship, though significant, is deemed of little importance quantitatively

THE DETERMINATION OF PARENTAGE. Kolmer has summarized the serologic aspects of the determination of disputed parentage.

Disputed parentage occurs in cases in which a man, named by a woman as the father of a child born out of lawful wedlock, denies such paternity, or in which a husband denies paternity of a child born in lawful wedlock Disputes involving maternity are much less common and usually involve a woman who has secretly secured a child for the purpose of compelling an alleged father to marry her, or to obtain dower rights in her dead husband's estate, or in order that the child may become the heir to her husband's estate. Disputes also arise occasionally in relation to the parentage of infants born in hospitals and accidentally interchanged, as well as in the case of wet nurses who willfully substitute their own infants for those placed in their charge, for the purpose of having their own secure the benefits of better homes.

Interpretation of Examinations of Blood. The agglutinogens, A, B, M, N, and Rh are transmitted by heredity. Examinations in relation to disputed parentage are based mainly on determinations of the major blood groups (O, A, B, AB) of the man, the

Kretschmer, will apply to all racial stocks. A somatic type that might be difficult to classify in one racial stock might be well within the limits of normal within another racial stock

VISCEROPTOSIS. In all of the racial stocks represented in the United States of America there is one somatic type, the visceroptotic, of common occurrence, which has caused much speculation in regard to diseases which have been considered incident to it.

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Visible peristalsis may occasionally be observed through the very thin abdominal wall if excessive gas is present in the intestine. In some patients the transverse colon is palpable It is doubtful whether anyone can palpate or observe visible peristalsis

nonpaternity cannot be proved. On the other hand, if the man belongs to group AB and the child to group O, or vice versa, nonpaternity is established, regardless of the group of the mother, although the chances of such proof are only about 5 per cent

The subgroups of A and AB corpuscles cannot be used for excluding paternity or maternity, but tests for the agglutinogens M and N give a man increased chances of proving nonpaternity. Men belonging to type MN, however, have no chance at all, whereas those belonging to M have 1 chance in 3, and in the case of N, 2 chances in 5. When the major blood groups and the subgroups M and N are determined at the same time, the chances of proving nonpaternity are significantly increased The chances of proving nonmaternity by determinations of the major blood groups alone are slight on account of the rare occurrence of AB, but maternity is disproved by any of the following four combinations. (1) alleged mother AB and child O; (2) alleged mother O and child AB; (3) alleged mother M and child N, (4) alleged mother N and child M.

If a child possesses agglutinogen M or N which is not present in the corpuscles of [illegible] is established. If either of the combinations, [illegible] ıan with type M child, is found, nonpaternity [illegible] s of particular importance when it is impos- [illegible]

The Rh-Hr blood types, however, have considerably enhanced the usefulness of blood tests in cases of disputed parentage, since these have increased the varieties of human blood that may be differentiated from 36 to 360. Under these conditions, an innocent man now has approximately a 50 per cent chance of being excluded when the tests are properly and skillfully conducted. Two Rh− parents can have only Rh− children. If one parent is Rh− and the other is Rh+, the children will all be Rh+ if the Rh+ parent is homozygous, or half the children will be Rh+ and half Rh− if the Rh+ parent is heterozygous. When both parents are Rh+, all the children will be Rh+ except when the parents are both heterozygous, in which case one fourth of the children will be Rh−.

Capacity for Resistance to Infectious Disease (Racial Susceptibility and Immunities). The genes in the human chromosomes control the capacities of the organism for actions and reactions in all spheres of activity including actions and reactions or susceptibility or immunity to microorganisms and viruses. Human beings by their varied manners of living in the past and at the present create environments which are to different degrees hospitable or hostile to the organisms of disease. The men and women who survived the vicissitudes of past environments did so because of a capacity to withstand infections. It does not seem unreasonable to believe that this ability to withstand infections influenced selection of somatic qualities just as much as did the rays of the sun, the temperature, and the altitude.

The spread of infectious disease depends on susceptibility of the host, the virulence of the disease agent, the number of contacts among individuals and the efficiency of their hygienic methods The capacity to resist disease is primarily physiologic, but certain anatomic attributes also are desirable, for instance a good pulmonary capacity in resistance to tuberculosis.

Resistance to infection is least during childhood and old age, when the sex hormones are not operative Sex hormones have much to do with immunization and resistance to disease. The slowly maturing individuals are relatively more vulnerable to infections for a longer time than are those who come to sexual maturity at an earlier age Thus, over the course of years, the slowly maturing, pinched-faced, weak-legged, narrow-chested, poorly co-ordinated adolescents tend to be discarded through natural selection. For example, it is Coon's impression that the prehygienic urban populations of the world, of the Near East, and the Mediterranean coast, and of the Inca and Aztec cities, were shorter, lighter, thinner-boned, and narrower-faced than those who lived in the surrounding country. The urbanites exhibited more asymmetries of body, thinner faces, and tended to have narrower noses than the ruralites. These undesirable anatomic weaknesses probably can be largely accounted for on the basis of poorer hygiene, less food, and more contacts and thus more infections among the urban dwellers than among their rural cousins. It seems

woman and the child. Examinations for the subgroups of A and AB corpuscles are not employed, but supplementary examinations for the agglutinogens M, N and Rh are of additional value and sometimes essential.

Table 16-1 shows what major blood groups are possible and what are not possible for the children of the various combinations of parents

Table 16-1. Possible and Impossible Blood Groups of Parents and Their Children

Groups of Parents	Groups of Children Possible	Groups of Children Not Possible
O x O	O	A, B, AB
O x A	O, A	B, AB
O x B	O, B	A, AB
O x AB	A, B	O, AB
A x A	O, A	B, AB
A x B	O, A, B, AB	—
A x AB	A, B, AB	O
B x B	O, B	A, AB
B x AB	A, B, AB	O
AB x AB	A, B, AB	O

From Kolmer, J A, Clinical Diagnosis by Laboratory Examinations, Ed 2, New York, Appleton-Century-Crofts, Inc, 1949, p 488

Agglutinogens A and B cannot be present in the corpuscles of a child unless present in the corpuscles of either or both parents A child of group O cannot have a parent belonging to group AB A child of group AB cannot have a parent belonging to group O

The tests may prove the nonpaternity of an accused man They cannot establish his paternity, however, because some other man of the same blood group may be the father. *If the man is AB and the child O, or vice versa,* nonpaternity is established regardless of the blood group of the mother If both father and child are A, nonpaternity cannot be established.

Table 16-2 shows what blood groups of the M-N series are possible and what are not possible for the children of the various combinations of parents.

Table 16-2. Possible and Impossible Combinations of Agglutinogens M or N of Parents and Their Children

Groups of Parents	Groups of Children Possible	Groups of Children Not Possible
MN x MN	MN, M, N	—
MN x N	MN, N	M
MN x M	MN, M	N
M x N	MN	M, N
M x M	M	MN, N
N x N	N	MN, M

From Kolmer, J A, Clinical Diagnosis by Laboratory Examinations, Ed 2, New York, Appleton-Century-Crofts, Inc, 1949, p 489

Men belonging to MN cannot prove nonpaternity If the child is M or N and these are absent in one or both parents, nonpaternity is established, also if the man is M and the child N, or the reverse

The chances of establishing nonmaternity by the major blood groups alone are slight *on account of* the rare occurrence of AB Maternity is disproved if an alleged mother is AB and the child O, or the reverse; also if the alleged mother is M and the child N, or the reverse.

In cases involving the parentage of infants accidentally interchanged in a hospital, or purposely exchanged by wet nurses, tests for agglutinogens M and N alone solve 40 per cent and tests for *agglutinogens A, B, M and N about 70 per cent.*

It may also be possible to make the grouping tests with the bloods of a man and a child as, for example, when a husband, suspecting his wife of infidelity, desires to obtain further evidence before making any charges If both man and child are found to belong to group A, it is useless to go further, since irrespective of the group of the mother,

Aside from dominant, recessive and sex-linked modes of transmission of disease, the possibility of mutation is to be considered. Mutations are of different kinds, and not all give rise to superiority of health and vigor Some result in what are known as disease and disability

In the practical application of these rules of genetics there is abundant evidence that many diseases of human beings are transmitted according to mendelian rule, but in most instances a genealogic analysis reveals a number of apparent discrepancies and irregularities which defy interpretation In part these discrepancies and irregularities can be accounted for on the basis of unknown genealogies which prevent accurate interpretations in diagnosis. Family genealogies are often unknown or inaccurate, particularly in regard to the undesirable members of the family, to illnesses and the cause of death.

Despite the smallness of human families the knowledge of forebears is limited. Less than 5 per cent of well informed human beings know the names of their great-grandparents. Fewer than 1 of every 10 patients know whether or not their grandparents had brothers or sisters. Much less knowledge therefore is available in regard to the health, sickness or disability which may have been present. For the foregoing reasons the occurrence of a given disease in a group of siblings without an accurate history of the same condition in ancestors cannot accurately be genetically interpreted. The diagnosis of a genetically recessive characteristic which is dependent on genes having a small incidence in the population—and it is only when two such genes are brought together by chance in the same individual that the disease assumes an overt form—may be difficult or impossible This speculation is supported by the observation that the mode of inheritance of a given disease may seem to change during several generations of the same family, and this cannot be explained except by splitting of the several pathologic genes in the manner mentioned. It is of practical diagnostic value to keep in mind that almost all sex-linked diseases behave like recessive characteristics

INTERNAL AND EXTERNAL CHARACTERISTICS

Body Odors. In the widespread contempt among the races, nearly every race is prone to charge all other races with being "smelly." A much publicized and somewhat dubious aphorism is to the effect that "we smell like what we eat" However, some races, apart from hygienic practices, exhibit odors which seem to be characteristic of themselves These odors are more readily perceived by individuals belonging to another race The Chinese and the Japanese, owing to their low nitrogen, cereal diet, are relatively free from any special racial odors. The Negro, both in Africa and elsewhere, seems to possess a distinctive body odor. The number of cutaneous glands conducive to offense is probably increased in this race. Among other groups, diet rather than an increased number of glandular elements may be the source of offense. Orientals complain of buttery odors of Europeans and of North Americans. Particularly, Orientals find difficulty in adjusting to the odors of European and American women The residents of Baltic regions are said to have a feculent odor The Eskimo smells like blubber even when the native dress has been abandoned The Brazilians are afflicted with body odors said to be Negroid in type but much less in degree The young and the old of any race are less odorous than the middle-aged The very lean and the very fat may be more offensive than those who enjoy normal nutrition, brunets more than blonds, women more than men Special acts and circumstances provoke the secretion of different odors within the sweat The menstruating woman or the pregnant woman may present odors apart from those associated with the genitalia

Bromhidrosis (Stinking Sweat). This disease of the sweat system also is termed osmidrosis. The disease may exist in spite of admirable efforts toward per-

from the evidence at hand that a poor grade of food and an unfavorable environment account for much of the so-called racial susceptibility to bacterial infections This is not true in the cases of viral and parasitic infections. The viral infections occur more readily in the well nourished than in the ill nourished. The parasites disregard the nutritional status of the host

Selection, Mutation, and Disease. The changes which occur in the genotype, and hence in its phenotypic expression in the individual, are controlled by selection Selection, however, does not originate changes of race or species New genes, or changes in the chemical composition of genes, are required for changes in race or species, and this is mutation

The exact cause of *mutation* is not known However, it was pointed out in the first part of this chapter that the influence of sunlight, cold, heat, humidity and altitude can change bodily function and influence anatomic structure There is no evidence that such factors ever influence the incidence of mutation, but the conditions present in the environment may be favorable to the life of certain mutants (dark skies for blondism) when they do occur and may thus perpetuate them If an attempt is made to weigh the molding influences of the environment against those of mutation and heredity, the result is to lose sight of the development of the individual as a whole. Premature conclusions in regard to the direct inheritance of physical characteristics, health or disease, or the acquired characters which have resulted from mutation in the environment, often lack the sort of judgment useful in diagnosis

The science of genetics teaches that heredity operates in orderly and predictable ways The expression of the genetic constitution is formulated by the mendelian rule

The mendelian rule implies that unit characteristics are transmitted in definite ratios by paired genes contained in the chromosomes of the germ cells Individuals receiving identical genes from each parent are termed *homozygous*, and those who have unlike genes, *heterozygous* Genes which always give rise to the characteristics which they convey are termed *dominant* Genes which are latent unless paired with identical genes from each parent are termed *recessive* The genes and the characteristics which they convey, which are contained within the same chromosome which determines sex, are designated *sex-linked*

Several instances of a given disease may occur among siblings despite the absence of a history of the same conditions in ancestors These sporadic occurrences may give the impression that the disease arises anew in each instance. According to the mendelian rule, however, this is to be expected of a recessive characteristic, which is dependent on genes having a small incidence in the population. When two such genes are brought together by chance in the same individual, the disease assumes an overt form For example, this is probably true in the sporadic instances of disseminated polyps of the colon.

When a disease behaves as a dominant characteristic in one family and as a recessive characteristic in another, there are among other interpretations the following possible explanations. (1) The disease is dependent on more than one pathologic gene, and these genes are closely associated in the chromosome and generally act as a unit but may become separated, so that a particular individual may not possess a complete set of these pathologic genes, but by chance mating the complementary genes necessary to produce the disease in overt form are obtained (2) The disease may occur as a dominant characteristic before the genes become separated and, after they are separated, may operate as a recessive trait

Probably another example of the splitting or the separation of genes is the apparent change in mode of inheritance of a given disease during several generations of the same family. Many of the sex-linked diseases behave like recessive characteristics. No sex-linked inherited disease of any type has been discovered which is restricted to and manifested only by the human female or which is even more frequent in the female than in the male.

In the realm of general and industrial toxicology, the probable cause of an affection or death may be disclosed by odors of the breath or the clothing or by odors emitted at necropsy. The worker in selenium, tellurium and arsenic has a garlic-like odor of his breath The odor of ethyl alcohol is readily detected. Errors may arise if too much emphasis is placed on the odor of alcohol on the breath, since the drinker, without being profoundly drunk, may be the victim of any of a long list of severe conditions leading to unconsciousness. Allyl alcohol, phenol and kindred chemicals, cresol, and lysol, sometimes used for purposes of suicide, possess revealing odors and thus facilitate diagnosis. The almond odor associated with hydrocyanic acid is so precise when present as to justify a working diagnosis of poisoning by a cyanide. In mercury poisoning the pronounced odor about the mouth is likely to result from stomatitis, but on rare occasions a metallic odor may be present Less frequently the same metallic odor may appear in lead poisoning In like manner odors may be associated with exposure to such other substances as carbon tetrachloride, trichloroethylene, gasoline, and benzol.

In the case of putrid odors from the *mouth*, difficulty may arise in determining the exact cause Gingivitis, stomatitis, purulent tonsillitis, Vincent's angina, bridgework, carious teeth, some pulmonary and gastric involvements—all may contribute a somewhat similar odor. The dentist, after drilling into an offending tooth, may be observed to sniff his drill after the dental canals have been reached. What he does after that may largely depend on the odor that he perceives. In some instances *ozena* (atrophic rhinitis) is accompanied by a foul and characteristic odor *Laryngeal diphtheria* in the necrotic stage emits a well-defined odor, but long before this period the diagnosis should have been made bacteriologically Such infections as typhoid fever, measles, scarlet fever and smallpox possess their own peculiar odors, none of which can be described as one apart from the others

Medicaments applied in the form of ointments, with ensuing absorption through the skin, may prove to be quickly injurious, and a diagnostic lead may be found in the lingering odor of the ointment

In rheumatic fever there has been described a highly differentiated odor of the skin set apart as sour or acid and said to be encountered in no other disease.

Gout is sometimes accompanied by an odor from the skin pathognomonic of that disease

The odor of *acetone* on the breath (apart from a worker employing acetone) immediately suggests the possibility of *diabetes* and calls for a more precise examination.

Figuratively speaking, a short path into the unconscious might be along the olfactory nerve In the *neuroses, inhibitions*, and *incompatibilities of marital life* disturbing odors may play an important but unrecognized role While these odors may not be accessible to the physician, an inquiry may reveal that odors are provocations for marital maladjustment

To a minor extent the absence of odor may attain medical import When fresh *feces* possess little or no odor, attention should be directed to the possibility of hepatic disease. In the presence of well-established jaundice the feces may be odorless.

The control of body odors comprises (1) systematic bathing and treatment for the curtailment of perspiration, (2) localized roentgen therapy and (3) local application of chemical antiperspirants and deodorants

Among active deodorants which operate by diminishing the flow of perspiration are the aluminum salts, particularly the chloride and sulfate, formaldehyde, alcohol, tannins and tannic acid, and iron salts (ferric chloride and others). Other materials such as zinc peroxide and oxide, hexamine, oxyquinoline sulfate, chloramine T, chlorthymol, and essential oils and perfumes act by nullifying the odor and are known as deodorizing agents.

sonal hygiene. All portions of the body may be involved in the productions c agreeable odors, but most blameworthy are the armpits, genital region, and A few persons may bathe the feet and change hose as many as four or five daily but still cause offense, chiefly to other persons, and an entire house, roo office may be made unlivable by the presence of one so afflicted.

The cause of this condition is not known, but it is oftenest associated with anemic, undernourished, alcoholic, or neurotic individuals. The state may be mittent. The offensive odors may long persist in a home or office after the p has departed

URHIDROSIS (Odor of Urine). The pathologic condition urhidrosis repr that abnormal state in which body waste ordinarily discharged in the urine l the body in perspiration, so that the offensive odor is that of urine and is c ammoniacal. The body odor encountered is not different from that of persons lack full control of the urinary bladder Any neglected infant presents the same not because of urhidrosis but because of wet diapers. This disorder may ar any person who has kidneys that are failing in their proper function. It rarely occur in otherwise perfect health

BODY ODOR-PRODUCING ORGANISMS Affections associated with abnorm of sweating may be the perfect ground for action of one or more bacteria, f or yeasts. Those bacteria which split urea, form indole, skatole, butyric acid, hy gen sulfide or other sulfur compounds, or any other odoriferous substances u certain conditions of growth on a particular cultural substance which may be pr in the surface or in the orifices of the body, may be expected to cause odors. *S tococcus foetidus* is the one species which has been given a special cognomen cating this quality

In any fungous infection, notably of the feet, offensive odors may be sev disturbing It is somewhat academic to set apart the extent of odors attribu solely to decomposing flesh in contrast to the fungi themselves. It neverthele mains that fungous disorders may be far more odorous than other affections of e severity in the same area. It appears probable that odorous offense from mem chiefly feet, may occur on a parasitic basis in the absence of open lesions. growth of such organisms in nearly normal interdigital macerated tissue may be cient to produce offensive odors. Persons who have such relatively innocuous i tions as tinea versicolor may present disturbing odors, chiefly associated with clot and recently occupied beds.

SIGNIFICANT BODY ODORS Olfactory diagnostic criteria continually were so out by physicians of former times. These physicians prided themselves that thr odor alone they were able to recognize such diseases as diphtheria, measles, monary abscesses, typhoid fever, leukemia, diabetes and some forms of insa and that by odors they could differentiate between many forms of "fevers."

It should not be inferred that the present-day diagnostician scorns odors in achievement of his diagnosis. Far from relegating odors to an outmoded past rating them as unworthy of a place in modern diagnostic methods, time and a every good diagnostician confronted with odors or their absence introduces evidence into his comprehensive appraisal For him, however, unlike his rem predecessor, acuity of the sense of smell is seldom a boasted prime implem Odors are now less important in diagnosis than formerly simply because i realized that the sense of smell is not in man, as in the dog, a dependable sense.

Odors as encountered in the work of the physician may reveal other th than a disease itself. The physician, through odors alone, records the impression t a patient is a tobacco user, an alcoholic, or given to low personal hygiene, that works in a certain trade or with certain chemicals, that she is menstruating, t certain drugs are being used in medication, or that certain foods have been ingest

Table 16-4. Height-Weight-Age Table for Boys *

Height, Inches	5 Yrs	6 Yrs	7 Yrs	8 Yrs	9 Yrs.	10 Yrs	11 Yrs.	12 Yrs	13 Yrs	14 Yrs	15 Yrs	16 Yrs	17 Yrs	18 Yrs	19 Yrs.
38	34	34													
39	35	35													
40	36	36													
41	38	38	38												
42	39	39	39	39											
43	41	41	41	41											
44	44	44	44	44											
45	46	46	46	46	46										
46	48	48	48	48	48										
47	49	50	50	50	50	50									
48		52	53	53	53	53									
49		55	55	55	55	55	55								
50		57	58	58	58	58	58	58							
51			61	61	61	61	61	61							
52			63	64	64	64	64	64	64						
53			66	67	67	67	67	68	68						
54				70	70	70	70	71	71	72					
55				72	72	73	74	74	74	74					
56				75	76	77	77	77	78	78	80				
57					79	80	81	81	82	83	83				
58					83	84	84	85	85	86	87				
59						87	88	89	89	90	90	90			
60						91	92	92	93	94	95	96			
61							95	96	97	99	100	103	106		
62							100	101	102	103	104	107	111	116	
63							105	106	107	108	110	113	118	123	127
64								109	111	113	115	117	121	126	130
65								114	117	118	120	122	127	131	134
66									119	122	125	128	132	136	139
67									124	128	130	134	136	139	142
68										134	134	137	141	143	147
69										137	139	143	146	149	152
70										143	144	145	148	151	155
71										148	150	151	152	154	159
72											153	155	156	158	163
73											157	160	162	164	167
74											160	164	168	170	171

From Duncan, G G, Diseases of Metabolism, Detailed Methods of Diagnosis and Treatment, a Text for the Practitioner Ed 3, Philadelphia, W B Saunders Company, 1952, p 1110

* Weight is expressed in pounds

An anthropometric survey of men and women in the U S. Army who were from 17 to 26 years of age revealed an average mean stature of the 17-year-olds of 67 71 inches (172 cm) and an average weight of 139 5 pounds (63 3 kg) After 1 or 2 years of service in the Army, the mean maximal stature of 68 51 inches (174 cm.) was attained at the age of 21 years; however, after the age of 19 years the average increase was only 0 1 inch (0.25 cm). The thoracic circumference for the 17-year-olds averaged 34 5 inches (87 6 cm) and for the 26-year-olds 36.76 inches (93 4 cm) The neck, judging from these measurements, appears to stabilize in the twenty-fourth year Of the extremities, the only measurement which showed any increase after 17 years of age was in the breadth of the hands, which showed an average increase of 2 per cent between 19 and 22 years of age.

The data from the Quartermaster Corps on the 17-year-olds resembles

Growth [illegible] is on a primary longitudinal [illegible] axis and to one another, [illegible] architectural plan, growth determined by [illegible] influences builds the somatic type of the individual Symmetry [illegible] the growing child are controlled by genetic factors Certain of these factors control physical growth in linear, others in circumferential dimensions.

A knowledge and understanding of the family background is a necessity in evaluation of size, for there is no doubt that body build is inherited and too is a reflection of the family and the racial background.

Average Weight and Stature of Youths and Young Adults. Average weights for given heights and ages of girls through the eighteenth year and boys through the nineteenth year are presented in Tables 16-3 and 16-4.

Table 16-3. Height-Weight-Age Table for Girls *

Height, Inches	5 Yrs	6 Yrs	7 Yrs	8 Yrs	9 Yrs	10 Yrs	11 Yrs	12 Yrs	13 Yrs	14 Yrs	15 Yrs	16 Yrs	17 Yrs	18 Yrs
38	33	33												
39	34	34												
40	36	36	36											
41	37	37	37											
42	39	39	39											
43	41	41	41	41										
44	42	42	42	42										
45	45	45	45	45	45									
46	47	47	47	48	48									
47	49	50	50	50	50	50								
48		52	52	52	52	53	53							
49		54	54	55	55	56	56							
50		56	56	57	58	59	61	62						
51			59	60	61	61	63	65						
52			63	64	64	64	65	67						
53			66	67	67	68	68	69	71					
54				69	70	70	71	71	73					
55				72	74	74	74	75	77	78				
56					76	78	78	79	81	83				
57					80	82	82	82	84	88	92			
58						84	86	86	88	93	96	101		
59						87	90	90	92	96	100	103	104	
60						91	95	95	97	101	105	108	109	111
61							99	100	101	105	108	112	113	116
62							104	105	106	109	113	115	117	118
63								110	110	112	116	117	119	120
64								114	115	117	119	120	122	123
65								118	120	121	122	123	125	126
66									124	124	125	128	129	130
67									128	130	131	133	133	135
68									131	133	135	136	138	138
69										135	137	138	140	142
70										136	138	140	142	144
71										138	140	142	144	145

From Duncan, G G, Diseases of Metabolism, Detailed Methods of Diagnosis and Treatment, a Text for the Practitioner, Ed 3, Philadelphia, W B Saunders Company, 1952, p 1111

* Weight is expressed in pounds

Some so-called pituitary dwarfs have hypoglycemic attacks which are probably due to deficiency (the gluconeogenetic factors) *of the adrenal In these a deficiency of* adrenal androgen is indicated by absence of sexual hair and decreased urinary excretion of 17-ketosteroids (less than 2 mg. daily).

Often in pituitary dwarfism no evidence of thyrotropic or adrenotropic failure can be detected, but lack of gonadotropic activity becomes conspicuous as the patients grow older. Usually there is a complete failure of sexual development. The testes or the ovaries remain small and immature and secondary sexual changes fail to appear. The urinary output of follicle-stimulating hormone is diminished (less than 6 mouse units per day). The absence of sexual hair, and the low values *for 17-ketosteroids and follicle-stimulating* hormone serve to distinguish cases of pituitary infantilism from hypogonadism due to primary ovarian or testicular deficiency.

Hypothyroid Dwarfism Dwarfism in hypothyroidism is characterized by stunting of growth and by delay in all the processes of maturation. Wilkins has observed that if the deficiency has existed from an early age, osseous development is retarded, infantile proportions of the upper and lower skeletal segments persist, dental development is retarded and the naso-orbital configuration retains infantile characteristics If thyroid deficiency does not develop until later childhood, when a more mature skeletal develop-

ed retardation

hypothyroid-

There is also

slow osseous development in patients who show delayed adolescent growth and development

Sexual Precocity and Dwarfism. Sexual precocity is at first manifested by an abnormally rapid rate of growth and osseous development, but premature fusion of the epiphysial lines usually causes cessation of growth before adult height has been attained In most cases of precocious puberty it is easy to explain the acceleration of growth on the basis of the early production of androgen However, rapid growth occurs in some cases of granulosa cell tumor of the ovary in which sexual development is due to estrogen elaborated by the neoplasm There is reason to believe that in such cases estrogen stimulates in turn the production of adrenal androgen, probably through its effect on the pituitary body

The common causes of dwarfism are severe and chronic disease occurring in childhood Almost any disease may stunt growth and, if sufficiently chronic, prevent development, and thus dwarfism ensues

Celiac disease, chronic ulcerative colitis, cystic fibrosis of the pancreas, renal disease such as polycystic kidneys and chronic nephritis, and hepatic disease or atresia of the bile ducts may be the cause of dwarfing Growth may be stunted without the appearance of any lesions of the bone Cardiac and pulmonary diseases which are accompanied by cyanosis often cause stunted growth

There are many children whose growth and sexual development are delayed Often but not invariably they have been smaller than the average throughout childhood and have consistently shown a delay of 2 to 4 years in their epiphysial development They remain sexually immature and continue to grow at a slow rate Their short height, lack of muscular development, and psychic immaturity, when they are compared with other children of the same age, make them more conspicuous at this time. Eventually puberty begins, but this may not occur until the patient is 16 or 17 years of age or older Adolescence may then progress rapidly, or there may be slow sexual development and somatic growth which may continue for a long time, owing to the fact that epiphysial ossification and fusion are delayed. Eventually these patients attain height within the normal adult range, although often they remain shorter than the average These differences in somatic and sexual maturation might depend on either genetic or nutritional influences affecting the entire organism, or on constitutional variations in the endocrine development and function of the individual That there is only a delay in growth and not a specific defect of some gland is shown by the fact that these patients eventually mature normally.

similar data obtained by the Brush Foundation over a 10-year period at Western Reserve University, Cleveland. The first period of the Brush Foundation studies covered fewer than 1,000 persons representing the economic group for which the average stature at age 17 years was 69.48 inches (176.5 cm.) and the average weight 147 5 pounds (66.9 kg.). The Army series at age 19 years, after 1 or 2 years of service, showed a mean weight averaging about that in the Brush series.

Dwarfishness (*Dwarfism*). A dwarf is an abnormally undersized person. Generally a person who has attained the age of an adult and who is less than 5 feet (152.4 cm) tall is a dwarf

Dwarfing may be hereditary in origin and dominant, as is revealed by the African pygmies It may occur sporadically in families The sporadic or the familial dwarf is often small at birth Growth is relatively slow from earliest infancy The centers of ossification appear at approximately the normal times and epiphysial union occurs normally The mental development is average. Sexual maturation takes place normally and at the usual time, and the features mature during adolescence. The child develops into a miniature but normal adult If the sporadic dwarf reproduces, the offspring are usually of normal size

Familial progeria with dwarfism (Hutchinson-Gilford disease) begins before the child is 1 year old. Between the onset and the age of 3 years, growth almost ceases and senile-like changes develop The features become sunken and drawn, the nose is thin and appears increased in length. The hair is thin and may be lost entirely Subcutaneous fat is lost The skin becomes atrophic and wrinkled There are deformities of the joints The epiphyses fuse prematurely In some cases there are arteriosclerosis and calcification of arteries Usually there is severe mental defect. The cause is unknown. It has been suggested that there are multiple genetic or germ plasm defects

Congenital absence of ovarian follicles has been observed in normal-appearing women (see Diseases of the Ovaries, Chapter 7). However, Wilkins has observed that a special type of genetic dwarfism is seen in the syndrome of ovarian agenesis and stunted growth Other congenital anomalies such as coarctation of the aorta, and defects of eyes and muscles are frequently present

In the syndrome of congenital ovarian agenesis, growth and development resemble those of the primordial, rather than the pituitary dwarf That is, epiphysial ossification is only slightly, if at all, delayed and epiphysial fusion occurs. The features mature as they ordinarily do during adolescence These patients do not have the childish facies seen in hypopituitary dwarfs The facial features are characteristically those of a mature woman with a poorly developed jaw and chin Frequently the diagnosis may be suspected from the facial appearance alone On examination these women have infantile sex organs.

Pituitary Dwarfism. Pituitary dwarfs are frequently of normal size at birth and during the first few years of life After [illegible]
cease entirely but usually continues at a [illegible]
opment, however, the epiphysial cente [illegible]
may fail to occur and the epiphysial lines may remain open or may close in adult life

The pituitary dwarf retains immature features and ages rapidly. In the twenties or the thirties, the skin may lose its elasticity and show aging but the features remain immature A lack of muscular development predisposes these patients to muscular asthenia and fatigability

It is rare that there are signs of tumor or other gross destructive lesions of the pituitary, such as changes in the sella turcica, constriction of the visual fields or evidence of increased intracranial pressure Dwarfism associated with xanthomatosis is of pituitary origin. Occasionally a craniopharyngioma or a glioma in the region of the optic chiasm or the hypothalamus may cause both dwarfing and diabetes insipidus In the absence of localizing signs pointing to a lesion in the pituitary region, proof that dwarfing is due to deficiency of the pituitary growth hormone depends on finding impairment of other pituitary functions. When a dwarf remains sexually infantile after adulthood, it is safe to presume that there is a deficiency of both the growth hormones and the gonadotropic hormones elaborated by the pituitary

The Cardiovascular System. Reduction in size and weight of the heart is by no means generally present in the senium. Atrophy of the striated muscle is not established with certainty Accumulation of lipochrome pigment within the muscle fibers takes place if the so-called brown atrophy occurs. The conduction system does not participate in any known senescent changes.

The changes in the endocardium and valves are those of atherosclerosis The valves lose their pliability because of an alteration of the texture of their elastic fibers, and deposition of fat and calcium. These changes are the most pronounced in the mitral and aortic valves

In the coronary arteries the elastic tissue and the ground substance of the intima are altered and eventually show deposits of cholesterol and calcium; in the media, however, deposits of calcium are rare.

The aorta loses its elasticity. This process leads to changes in the configuration of the aorta, and is most marked in areas exposed to special strain

As the atherosclerosis advances in the arteries, the elastic membrane of the intima splits, the elasticity of the vessel wall deteriorates, and deposits of calcium accumulate in the media.

Symptoms Prior to angina pectoris or congestive failure there are no distinct symptoms indicative of the aging heart

Examination The rate of the heart beat, after decreasing between birth and the tenth year of life, remains at a plateau from the third to the fifth decade. Thereafter, another slight slowing may occur in some persons. The rhythm of the pulse may be changed Premature contractions may be observed.

Electrocardiograms of older persons appear to some investigators to be indicative of significant changes Most cardiologists do not find electrocardiographic changes which are indicative of advancing years.

The cardiac output in men between 40 and 90 years of age reveals no evidence of decrease in discharge of blood referable to age.

Reduction of arterial elasticity as expressed in the quality of the pulse reflects the passive expansion and elongation of the arterial walls There is a relationship between elasticity and velocity as expressed in a greater rise in systolic blood pressure in less elastic arteries in response to the same cardiac output

The changes in blood pressure as age advances have been described in the section on hypertension The systolic blood pressure gradually rises without significant change in the normal limits of the diastolic pressure

The Urinary System. Arteriosclerotic involvement of the kidneys is common from middle age on. The parenchymal changes are referable to the vascular affections present Reduced blood supply to the renal parenchyma engenders the ischemic tissue reaction of simple atrophy characteristic of the slow progress of the vascular changes The number of functioning glomeruli is reduced in accordance with the degree of vascular change.

The elimination of metabolites under ordinary conditions remains unimpaired when sufficient functioning tissue is left in the kidneys. Extensive arteriosclerotic changes in the kidneys and the disease resulting therefrom are not characteristic of aging

The Reproductive System The changes of the genitals incident to advancing years have been described in the consideration of diseases of the reproductive organs Essentially these changes are shrinkage except in the case of the prostate gland, in which the change is one of hypertrophy.

The Nervous System. The pathologic changes that take place in the central nervous system are extensive. The extreme effects of the senium may leave the leptomeninges thickened and the seat of cavitation or focal gliosis.

The brain may be shrunken and unduly hard; the sulci are deepened and widened, especially in the frontal lobes The ventricles dilate, and their walls become

Diagnosis of Dwarfishness. Generally one type of dwarf cannot be distinguished from another on the basis of the size which the patient attained at some particular time before puberty. It is necessary to wait to learn what finally happens in regard to sexual development.

The diagnosis of dwarfism due to disease of bone depends on the roentgenographic findings and the absence of signs of endocrine dysfunction. The diagnosis of dwarfism due to severe chronic diseases which occurred in childhood (for example, rickets) depends on diagnosis first of the chronic disease which caused the dwarfism.

The correction of nutritional and metabolic disturbances usually leads to a resumption of growth when these factors are the primary cause of stunting. Refractory rickets is sometimes susceptible to treatment, with striking improvement in growth In hypothyroid dwarfism the response to administration of thyroid is very gratifying.

Gigantism. In the discussion of diseases of the pituitary gland in Chapter 14 it is mentioned that the diagnosis of gigantism is exceedingly difficult in the borderline case. Hyperactivity of the anterior lobe of the pituitary results in gigantism when the condition occurs in the adolescent, and in acromegaly when present in the adult. In all instances of gigantism due to hyperfunction of the pituitary, eventually the features of acromegaly develop The main point in the differential diagnosis between the genetic giant and the pituitary giant is the evidence obtained from the genealogic history plus the final development of the features of gigantism

The Senium. Feebleness of mind and body accompany advancing years There are no criteria for the prediction of the age at which feebleness will begin The best evidence indicates that aging begins with birth and progresses thereafter. It has become the custom of the medical profession to yield to the arbitrarily set age of 65 years as being the time that men and women are unfit for use. This arbitrary fixing of any age as the point at which there will be an end to the productive capacity of men and women is impossible to square with medical and historical facts concerning the accomplishments of aged men and women. Michelangelo finished painting the Last Judgment at the age of 66 years He completed frescos in Pauline Chapel in his seventy-second year After this he devoted himself to architecture and engineering until his eighty-ninth year despite fever, gallstones and gout.

Practically all of the symptoms and signs attributable to advancing years accompany arteriosclerosis and atherosclerosis These diseases may begin at any time in life, and if men and women are to be retired on account of the symptoms incident thereto, the retirement age should in some instances be at 40 years instead of 65 years and in others the number of years is not significant of capacity for work.

Most men and women mellow with age. They become docile and agreeable and philosophically inclined and are a wholesome influence on their friends and families. These men and women seem to have escaped the attentions of the medical profession, for they are rarely mentioned They do not need to consult physicians

Owing to the fact that the age of a person cannot be adequately expressed in biologic units which would indicate the physiologic age, it is realized that the complaint, the symptoms and the physical findings in the aged may be, although they rarely are, different from those in the younger age groups who have comparable diseases. For the sake of convenience, old age may be defined as the stage of life which extends from some time in middle life to the eightieth year. From 80 years on, advanced old age prevails.

With increasing age, body length decreases This change is partly real, owing to atrophy of the intervertebral disks, and partly illusory, resulting from an increasing forward bending of the spinal column and flattening of the plantar arches as the result of loss of muscular tone. Reduction in weight of most tissues and organs prevails with the advancing years.

Ménière's syndrome, suggests a lesion of the brain stem and is not a common complaint. Giddiness among elderly persons, like this symptom in younger persons, is often functional In some there may be an increased sensitivity of the carotid sinus.

In Woltman's experience in a series of 200 cases the disorders of elderly patients which were referable to the nervous system were, in the order of frequency of occurrence, disease of peripheral nerves, cerebral arteriosclerosis, psychiatric disturbances, residua of major vascular insults, major neuralgias, convulsive disorders, headache, parkinsonism, brain tumor and syphilis of the nervous system. The common complaints expressed by relatives in regard to these patients pertained to psychiatric disturbances Many of such patients are segregated at home because of conduct intolerable from a social point of view.

The symptoms of disease in the aged may not be fully manifest because of the pathologic changes in the brain The high incidence of neurosis is the same in the aged as in younger persons. Woltman observed, in the cases mentioned, that the same familiar neurotic complaints had been recorded in the histories of these same patients thirty or more years prior to the examination

Prior to a stroke there may be dull, persistent, unilateral pain. It may include half of the body or only part of it, especially the proximal part of a limb and the adjacent part of the trunk. This "thalamic syndrome" fluctuates greatly in intensity with the mood of the patient.

Pseudobulbar palsy may be a gradually acquired disability and complaint.

Gastrointestinal neuroses, depressive reactions, chronic fatigue states, anxieties, melancholia, headaches and giddiness all may be related to the aging process

EXAMINATION The commonest physical manifestations observed in the aged [illegible]

[illegible] impaired functions of nerves, muscles and bones The identification of Parkinson's [illegible]

[illegible] ances in gait may be observed such as walking with short steps and a distinctive hesitation and uncertainty of gait while walking Apparent locomotor difficulties may arise from poor vision

The pupils are often somewhat irregular and sluggish in their reactions, and conjugate movements of the eyeballs upward may be limited The oculi fundi may reveal evidence of arteriosclerosis. Cataracts and choroidal degenerations and arcus senilis are common The most distinctive evidence of advancing age in the eye is the loss of the bright hue to eye color The eyelashes and the eyebrows are apt to be coarse and out of control as the result of excessive growth

Impairment of hearing, especially for high tones, is common. Impairment of hearing may account for an apparent inattention and preoccupation.

The lack of co-operation during the examination of an aged patient may be the only objective finding Co-operation, particularly in the sensory tests, is poor, these patients either fail to answer or else give the same answer to all questions or stimulations Irritability may be manifest in some. Emotional instability is frequently observed in the aged However, it must be emphasized that it is commoner to find the aged more stabilized emotionally than they were when they were younger

The inability to sustain attention is often the basis for defects in memory. The memory often is clear for remote events but poor in recalling current events. Aphasias in both sensory and motor spheres are common if evidence of cerebral arteriosclerosis is present.

There is often unsteadiness in the Romberg position. In some patients there is no appreciation of vibratory sensations, and in a few a loss of appreciation of move-

rough and ridged The cortical lopographic configurations become thinner and less distinct than usual; the white matter and the deep nuclei are shrunken.

The nerve cells are atrophied, laden with pigment, vacuolated, and decreased in number, and their processes are reduced in number and replaced by gliosis. Corpora amylacea and senile plaques are common, as are also changes in the choroid plexus.

In the spinal cord there may be a marginal pallor, especially of the fasciculus gracilis

Arteriosclerosis is not invariably present in old age, but when present it involves especially the large vessels (atherosclerosis) of the base and pia In larger vessels of the brain the alteration is chiefly atherosclerotic. The vessels on the whole become *roughened, tortuous and hardened and unyielding, therefore, they may* indent neuronal structures such as the optic chiasm, the atheroma may ulcerate, set free an embolus, or form the site of a thrombus, an aneurysm or a hemorrhage. However, rupture of the larger vessels of the base of the brain is rare in the absence of aneurysmal formation. Advanced changes of the blood vessels of the brain may be present without clinical manifestations

In the peripheral nerves there may be a reduction in the number of fibers and an increase in the supportive tissues Aging persons have more discomfort attributable to the peripheral nerves than do younger people Feelings of numbness, paresthesias and pains in the course of one or more peripheral nerves may be the source of great worry in the senium

Essential hypertension in middle life reduces the size of the lumen of the arterioles, progressing to involve the smaller arteries. This gradual closure of the smaller arteries reduces the quantity of blood which can be delivered to the tissues. Reduction of blood supply causes reduction in function of the tissue deprived of adequate amounts of blood. The manifestation of this slow starvation of the tissue consists of loss of function without pain The closure of the lumen of an artery of medium size by a thrombus, for instance, a leg artery, is manifested by pain and often sudden death of the tissues distal to the closure if the collateral circulation is not adequate. Closure of the arteries in the aged person is common due to the reduced, roughened, irregularly sized lumen of the vessel. The reduction in the size of the lumen is produced by atherosclerosis incident to aging

SYMPTOMS. The chief complaint of many aged patients is weakness On inquiry, however, the physician learns that the basic difficulty is not weakness but impairment in use of the lower limbs because of pain, ataxia, spasticity, or a tremor Often the pain is of skeletal origin and not due to vascular disease When it is due to atherosclerosis it takes the form of claudication The spasticity is characteristic of pyramidal neuron lesions and is a part of a Parkinson syndrome due to vascular disease in the brain The tremor has been present for years, especially under conditions of fatigue, and other members of the family have been affected *similarly In* most instances tremor in the aged as in younger persons is heredofamilial and not of vascular origin unless it too is a part of a Parkinson syndrome.

Impairment in memory is often the chief complaint On analysis it is often obvious that the imperfections of memory are due to poorly sustained attention, which is often greater than the patient's general behavior suggests.

Headache, bregmatic or frontal in situation, and generally of a dull heavy type, but sometimes *stabbing and sharply localized and not greatly influenced* by straining or jarring of the head, may be a complaint

Aging patients may have a persistent symmetric burning of the tongue and *inside* [illegible] findings, to which has been given [illegible] occurs in women more than the age [illegible] with depression, and not to age.

A commonly occurring [illegible] Intense vertigo, like that of

one or more of the operators of the motor vehicles involved or in the pedestrian when the latter is affected These personal factors comprise: (1) Temporary or permanent physical or mental deficiency prevents the involved person from being able to do any better One or more of the operators or the pedestrian has not had the proper experience, skill or training in protection of himself from physical harm, or if he has had such experience and training, he may have lost such as the result of accident or disease or through the normal processes of age. (2) The most important group of persons involved in accidents includes those who profess not to want to have an accident but who maintain a careless, reckless, inattentive and generally faulty attitude. They are inherently awkward, often preoccupied with emotional and neuromuscular tensions, and are afflicted with feelings of hostility or guilt

The somatic defects which prevent proper action or which may interfere with a person who is operating a motor vehicle may be classed as follows: (1) diseases which affect locomotion or the mechanical structures of the body including bones, joints and muscles, and peripheral vascular or peripheral nervous structures; (2) diseases of the cardiovascular, respiratory, hemic, lymphatic, digestive, urogenital, endocrine and nervous systems; (3) diseases of the organs of special senses.

The influence of the nerves, as controlled finally by the cerebrum in the operation of a motor vehicle, is that ability to perform synchronizing, smooth, steady acts and movements resulting in proficiency, deftness and good control. These are the organized habits of the motor and sensory nerves which have been gained by a lifetime of cultivation and by correction of many awkward movements incident to learning to perform skilled acts The loss of these organized habits of motor function may be the result of interruption of the functions of the motor nerves, as occurs in a host of diseases of the peripheral nerves (injury), of the spinal cord (poliomyelitis), injury of the cerebellum as in ataxia (tumors, birth injuries, vascular disease), lesions of the basilar nuclei of the brain (extrapyramidal neurons as in Parkinson's disease), and diseases or injury of the cerebral cortex which result in an inability to initiate movement Likewise an interruption of the function of the sensory neurons interferes with the performance of co-ordinated movements, many times because of inability to know where the part is or how far to move it, as occurs in locomotor ataxia

These aberrations of function of the nervous system in disease can be easily recognized even if not diagnosed They are permanent and progressive and once established should prohibit their victims from operation of motor vehicles.

The interruption of synchronized, smooth, steady movements which result in proficiency, deftness and good control is more frequently due to narcotic and sedative drugs than to disease. The chronic addiction to alcohol or drugs, or the immediate acute effects of these drugs, produce awkwardness incompatible with performance of the movements of organized habits of the motor and sensory nerves These conditions are definite indications for not operating a motor vehicle.

Diseases of the cardiovascular system, especially in aging persons, may influence the ability to operate a motor vehicle. These diseases often interfere with the functions of (1) the brain, manifested by symptoms such as amnesias, aphasias, encephalopathies, and hemiplegias, (2) the heart, manifested by angina pectoris and coronary occlusions, (3) the extremities, manifested by arterial spasm, as in Raynaud's disease and Raynaud's phenomenon, and occlusive arterial disease, such as is present in atherosclerosis and in endarteritis obliterans or thromboangiitis obliterans.

A sufficient degree of amnesia may be reason to forbid a patient to operate a motor vehicle Aphasia, either motor or sensory, and hemiplegia disqualify one for the operation of a motor vehicle. The rest of the cardiovascular diseases are rarely

ments of the joints is present. The tendon reflexes may be unequal or absent. The plantar response may be plantar extension (Babinski's sign). Impairment in superficial sensibility and, occasionally, evidence of degeneration of anterior horn cells are common findings if the attention of the patient can be maintained long enough to test for these abormalities. The urologist may find a cord bladder to account for urinary symptoms.

DIAGNOSIS The diagnosis of the senium, the feebleness of mind and body incident to old age, cannot be made unless such signs and symptoms are present. There is no age at which these may be expected to be present In many aging men and women the usual manifestations of aging are never present. More commonly men and women gradually slow down with the advancing years, they shrink up bodily and become mellow and placid mentally, and seek, not the physician, but spiritual comforts These men and women are not the subjects for medical reporting, for they are not seen by physicians. They have formed, in the past, a great stabilizing influence on society The future, with a promise of enforced retirement, threatens to deprive society of this desirable heritage, since these men and women will be uprooted, so to speak, and cast away Many of them will not have the solace of interests because they have not had time to do anything more than their daily work

QUALIFICATIONS OF OPERATORS OF MOTOR VEHICLES

In a broad classification of motor vehicle accidents there are those due to (1) adverse road conditions, (2) mechanical failure of the vehicle and (3) the human factor, the operator. Here the interest is in the human factor.

There are various groups of operators of motor vehicles and these are determined by the use of the motor vehicle, for instance, whether the vehicle is engaged in transportation in the public interest or whether it is owned and operated for private use in business and in pleasure. In practice, the physician is aware that the physical and mental qualifications of an operator of a cab or a semitrailer should be much different from those of the farmer who operates a one-half ton truck for use on the farm and for going to town and to church Between the qualifications of the operators of vehicles in the public interest and those of the certain farmers whose qualifications comprise the ability to start, steer and stop their vehicles are the qualifications of the numerous persons who own and operate their own vehicles for business and pleasure.

Among the persons who consult the physician of their own volition or those referred to the physician by members of their own families or by officers of the law in regard to their qualifications to operate a motor vehicle it is evident that there are those who have had more motor vehicle accidents than others Certain variations in the number of accidents a given person has are permissible if the number of accidents falls within the limits permitted by a simple algebraic law (Poisson's law)

In recent years it has been repeatedly demonstrated that some persons have more than their share of accidents as permitted by Poisson's law Permanent somatic weaknesses or deformities are not the cause of the excessive number of accidents that these persons have. The National Safety Council's statistical yearbook *Accident Facts* (1948) reveals that bodily defects, visual and other, were reported as a cause in only 2 per cent of some 5,000 accidents analyzed. "Improper attitude" was reported in 50 per cent of the cases, "a lack of knowledge or skill" in 30 per cent and "no personal cause" in 18 per cent It is evident, therefore, that there is an individual human element in those who have accidents, and motor vehicle accidents are no exception to this rule

In all instances of motor vehicle accidents etiologically the personal factors are by far the most important. In most accidents there are personal factors present in

the semicircular canals, such as may occur in Ménière's syndrome, may be of sufficient degree to disqualify for the operation of a motor vehicle.

The proper official, in many states, may require an aging person, on renewal of a driver's license, to take an examination, as upon the original application, and so notifies him by letter. The aging person brings such a letter to the physician for advice. It is the physician's duty personally to conduct the specific examinations with regard to the applicant's physical and mental condition and if the results are satisfactory, to find out who notified those who issue drivers' licenses that the patient was incompetent; often the licensing office has been notified by some "friend" or relative or member of the patient's immediate family that it is unsafe "at his age" to operate a motor vehicle The physician can then act promptly and correctly, for the physician knows that most persons drive for a lifetime without a serious accident. If age brings some impairment of vision and some slowing of mental and physical response, they drive more carefully and more slowly, not necessarily because they have become converts to safety but simply because it is more comfortable Age alone, or rather the number of years a person has lived, is never in itself a disqualification for the operation of a motor vehicle. A tottering old man, who may be 50, 60, or 80 years of age, should not be sanctioned by the physician as being physically fit for the performance of any duty that might endanger his own life or the lives of others.

The age at which a youth may safely operate a motor vehicle is variable This age is often arbitrarily set by law in the neighborhood of 16 years The skillful young driver can take chances that the elderly driver cannot take; conversely, the careful driver can get along with slower reactions and less perfect vision than can the careless operator Thus it is difficult to set definite standards for any one of these many variables. To date, the best measure of the person's ability as a driver is his or her own accident (and near-accident) record, irrespective of the age

The psychologic factors which interfere with the safe operation of a motor vehicle pertain to the so-called accident proneness of the person. Accident proneness may be inborn or acquired When the quality is inborn, the subject has an accident when an accident prone situation is met. These persons unconsciously have purposive accident tendencies as expressions of hostility or guilt Any person may become accident prone if he operates a motor vehicle when he is preoccupied by emotional and neuromuscular tensions, if fatigue or severe pain is present, if stung by a bee while driving, or if under the influence of alcoholic liquors or narcotics or atropine

All persons [illegible] of high velocity [illegible] [illegible]ds, are accident [illegible] is increased by the presence of excessive fright Likewise accidents are likely to be more serious to those who are not fearful of such hazards than to those who are aware of danger.

The Operation of Motor Vehicles by Drivers Under the Influence of Alcohol. The action of small amounts of alcohol on the central nervous system has assumed great importance owing to the increased numbers of automobiles in use and the high speeds at which they are driven Impaired judgment and slowed reflexes may make all the difference between safety and death on the public highway The danger is especially great since alcohol disappears from the blood relatively slowly, and its action, therefore, persists much longer than is generally recognized It should be understood that for such use of alcohol the terms drunkenness and intoxication are not appropriate The best term is under the influence of alcohol.

Courts of law have had considerable difficulty in deciding cases of accidents in which alcohol has been claimed as a contributory factor, and physicians have not been able to help as much as it is desired in arriving at decisions Chemical tests

of a nature to disqualify for the operation of a motor vehicle unless there is the habit of recurring severe pain.

There are two groups of patients who have habitual loss of consciousness who should not operate a motor vehicle. (1) epileptic persons and (2) those who have extremely hypersensitive carotid sinuses. An epileptic person's sensorium is dulled by the action of sedative drugs. In addition to this, a seizure may come on without a recognizable aura so that caution for protection of himself and others cannot be taken. The person who has a very sensitive carotid sinus may momentarily lose consciousness by a quick turn of the neck, especially if tight neckwear is worn.

A third group of patients who must be considered respectively, and on the basis of their individual histories, comprises diabetic patients, who may have insulin reactions, and those who have hyperinsulinism

Diseases of the hemic system, except from weakness, do not prevent the patient from driving a car. Massive lymphedema such as may occur occasionally in the feet and legs causes a morbid degree of awkwardness Likewise diseases of the digestive system, except for the subacute and chronic dysenteric diseases such as chronic ulcerative colitis and acute, painful, thrombosed hemorrhoids of a severe degree, are not contraindicative for operation of a motor vehicle

Despite a lack of statistical evidence, it is generally believed that eyesight is an important attribute for operation of a motor vehicle, and physical examination for a driver's license usually includes tests of vision or requires the applicant to furnish proof of fair vision with or without the use of glasses These examinations include acuity as tested by means of a Snellen chart. An acceptable safe level at which to grant general driving privileges is 20/40, though opinion in the various states differs, so that levels from 20/30 to 20/70 are accepted

If the applicant must wear glasses in order to pass the tests, his license is ordinarily restricted to driving with glasses If he fails to meet the 20/40 test he may consult a specialist on vision and then have a retest Even if he then fails, he may still, after special study, be given a restricted license permitting him to do the kind of driving he is "able to do in reasonable safety" Some drivers who have visual acuity of 20/200 and even lower, have demonstrated their ability to drive safely under certain limited circumstances The AAMVA standard further says. "The screening standard, therefore, is a flexible rather than fixed standard"

Tests for color vision utilize either colored materials or the Ishihara chart. Color blindness is a hazard in traffic only if the driver is unable to distinguish red from green, or rather to discriminate between the yellow-red and blue-green used in traffic signals Even this is not so important today when nearly all such signals have been standardized, with red at the top and green at the bottom

In the operation of a motor vehicle a phoria may be important.

Restricted visual field is a hazard in operation of motor vehicles, particularly in right angle collisions, unless the driver recognizes his deficiency, drives more slowly when approaching an intersection, and turns his eyes or even his head to see what is coming. As in other items, the danger lies in unawareness of the defect quite as much as in the defect itself.

Tests of night vision appear not to have been developed to the point at which it would be feasible to undertake such procedures Satisfactory night vision includes the ability to see well with low illumination, ability to see against glare, and a rapid recovery from glare blindness

Generally, defective hearing plays little if any part as a cause of unsafe operation of a motor vehicle. Those who have defective hearing have developed a sharp visual alertness. The handicap of defective hearing is not a road hazard but may be hazardous to the motor vehicle, for the operator may not hear the noise created by mechanical imperfections in the vehicle and thus the machine may be severely damaged because of continued use after trouble has developed Disturbances of

the semicircular canals, such as may occur in Ménière's syndrome, may be of sufficient degree to disqualify for the operation of a motor vehicle.

The proper official, in many states, may require an aging person, on renewal of a driver's license, to take an examination, as upon the original application, and so notifies him by letter. The aging person brings such a letter to the physician for advice. It is the physician's duty personally to conduct the specific examinations with regard to the applicant's physical and mental condition and if the results are satisfactory, to find out who notified those who issue drivers' licenses that the patient was incompetent; often the licensing office has been notified by some "friend" or relative or member of the patient's immediate family that it is unsafe "at his age" to operate a motor vehicle. The physician can then act promptly and correctly, for the physician knows that most persons drive for a lifetime without a serious accident. If age brings some impairment of vision and some slowing of mental and physical response, they drive more carefully and more slowly, not necessarily because they have become converts to safety but simply because it is more comfortable. Age alone, or rather the number of years a person has lived, is never in itself a disqualification for the operation of a motor vehicle. A tottering old man, who may be 50, 60, or 80 years of age, should not be sanctioned by the physician as being physically fit for the performance of any duty that might endanger his own life or the lives of others.

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The psychologic factors which interfere with the safe operation of a motor vehicle pertain to the so-called accident proneness of the person. Accident proneness may be inborn or acquired When the quality is inborn, the subject has an accident when an accident prone situation is met. These persons unconsciously have purposive accident tendencies as expressions of hostility or guilt Any person may become accident prone if he operates a motor vehicle when he is preoccupied by emotional and neuromuscular tensions, if fatigue or severe pain is present, if stung by a bee while driving, or if under the influence of alcoholic liquors or narcotics or atropine

All persons caught in severe inclement weather such as winds of high velocity (30 miles per hour or more), rain, or snow, or on icy or muddy roads, are accident prone. The likelihood of accidents under these adverse conditions is increased by the presence of excessive fright Likewise accidents are likely to be more serious to those who are not fearful of such hazards than to those who are aware of danger.

The Operation of Motor Vehicles by Drivers Under the Influence of Alcohol. The action of small amounts of alcohol on the central nervous system has assumed great importance owing to the increased numbers of automobiles in use and the high speeds at which they are driven. Impaired judgment and slowed reflexes may make all the difference between safety and death on the public highway. The danger is especially great since alcohol disappears from the blood relatively slowly, and its action, therefore, persists much longer than is generally recognized It should be understood that for such use of alcohol the terms drunkenness and intoxication are not appropriate. The best term is under the influence of alcohol.

Courts of law have had considerable difficulty in deciding cases of accidents in which alcohol has been claimed as a contributory factor, and physicians have not been able to help as much as it is desired in arriving at decisions Chemical tests

for alcohol in the blood or the urine may be employed for such purposes, for behavior reactions can be correlated with the alcoholic content of the body fluids.

However, evidence obtained from analyses of the blood or urine is not admissible in the courts of law because such evidence, if positive, would violate the individual's rights guaranteed by the Fifth Amendment of the Constitution of the United States unless permission was granted for its use.

With reference to the operation of a motor vehicle, when there is less than 0.05 per cent of alcohol in the blood, or equivalent amounts in the other body fluids or in the breath, the subject should be presumed to be not under the influence of alcohol. The presence of 0 15 per cent or more in the blood is presumptive evidence that the subject is under the influence of alcohol If the blood content of alcohol is between 0 05 and 0.15 per cent, other tests and observations must be taken into consideration in determining the degree to which the subject is affected The average adult must ingest at least two 12 ounce bottles of beer or 2 ounces of 100 proof whiskey for the blood to contain 0 05 per cent alcohol

In general, the concentration of alcohol in the blood is 1.2 times as high as in the brain, 0 8 as high as in the urine, and 2,000 times as high as in the expired air It reaches its maximal level in the blood within an hour after ingestion and is oxidized at the rate of 0.15 to 0.185 gm per kilogram of body weight per hour Even small doses will affect adversely rapid and accurate co-ordination

Accidents may be used to bring about dependence and compensation either in the form of sympathy or financial return. They may be the result of fatigue and falling asleep at the wheel.

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17

COMMUNICABLE AND INFECTIOUS DISEASES

The infections and communicable diseases which usually remain confined to a topographic area, an organ or a system have been described in their appropriate places. For instance, communicable diseases which affect the salivary glands, the organs of locomotion, the genitalia, the skin, the respiratory passages, the digestive system, the liver, or the cranial portion of the central nervous system have been described under the respective organs or systems.

It is now proposed to describe some disorders caused by diverse microscopic and ultramicroscopic organisms which are disseminated through the lymph or blood streams and which are characteristically manifested by fever and are usually communicable

Communicable Diseases. A communicable disease is one capable of being transmitted from one person to another It is re-emphasized that not all communicable diseases are considered here At this time there are two categories of communicable diseases under discussion and both of these are characterized by widespread dissemination through the body by the lymph or the blood or both. These categories are (1) Those organisms like the streptococcus and the staphylococcus which can be communicated from one person to another and which usually originate only a localized infection However, these organisms are capable of passing the local barriers to infection and on into the lymph or blood streams and then cause widespread foci or generalized disease (2) Those organisms which immediately pass from the portal of entry into the lymph and blood and cause localized disease depending on their tropic properties subsequent to dissemination. In the first category the disease originates at the portal of entry of the infecting organism and subsequent to the original local infection there is a bacteremia or septicemia. In the second category there is no disease or at most minimal disease at the portal of entry

Transmission of Communicable Diseases. The bacteria, some of the viruses and higher plant organisms are passed from one host to another on dust particles, drops of sputum or nasal secretions These means of transmission of infection are designated air-borne Infections transmitted by food or drink are said to be transmitted by indirect conveyances. Direct infections ensue from corporal contacts, use of common utensils, clothing or linens Some viral, rickettsial, and parasitic diseases require mechanical or biologic vectors for their transmission The biologic vectors are often arthropods

The Control of Communicable Diseases. There are certain diseases due to plant and animal parasites or to filtrable viruses and rickettsias which are easily communicable from one person to another These diseases are designated communicable diseases, and notification of their presence in a community to the local or state health departments is required and may be mandatory by law.

The following lists of communicable diseases have been taken from Reprint No 1697 (revised, 1950), Public Health Reports, prepared by the United States Public Health Service.*

* Included here by permission of the United States Public Health Service

LIST OF DISEASES OF WHICH NOTIFICATION IS REQUIRED

Actinomycosis
Amebiasis
Anthrax
Bartonellosis
Boutonneuse fever
Brucellosis (undulant fever)
Chancroid
Cholera
Conjunctivitis, acute infectious (of the newborn, not including trachoma)
Dengue
Diphtheria
Dysentery, amebic
Dysentery, bacillary
Encephalitis, infectious (lethargic and nonlethargic)
Favus
German measles (rubella)
Glanders
Gonorrhea
Hepatitis, epidemic
Hepatitis, serum homologous
Hookworm disease (ancylostomiasis)
Influenza
Keratoconjunctivitis, infectious
Leprosy
Malaria
Measles (rubeola)
Meningococcus meningitis (cerebrospinal fever)
Mumps (infectious parotitis)
Paratyphoid fever
Plague, bubonic, septicemic, pneumonic
Pneumonia, acute lobar
Poliomyelitis
Psittacosis
Puerperal infection (puerperal septicemia)
Q fever
Rabies
Rickettsialpox
Rocky Mountain spotted (or tick) fever
Scarlet fever (scarlatina)
Septic sore throat
Salmonellosis
Smallpox (variola)
Swimming-pool conjunctivitis
Syphilis
Tetanus
Trachoma
Trichinosis
Tuberculosis, pulmonary
Tuberculosis, other than pulmonary
Tularemia
Typhoid fever
Typhus fever
Whooping cough (pertussis)
Yellow fever

COMMUNICABLE DISEASES OR INFESTATIONS OCCURRING IN THE UNITED STATES AND INSULAR POSSESSIONS, BUT FOR WHICH NOTIFICATION TO THE HEALTH AUTHORITIES IS NOT EVERYWHERE REQUIRED

Ascariasis
Chickenpox
Coccidioidomycosis (coccidioidal granuloma, "valley fever")
Common cold
Enterobiasis
Filariasis
Hemorrhagic jaundice (spirochetosis icterohaemorrhagica, Weil's disease)
Histoplasmosis
Impetigo contagiosa
Lymphogranuloma venereum (inguinale) and climatic bubo
Pediculosis (lousiness)
Rat-bite fever
Relapsing fever
Ringworm (dermatophytosis)
Scabies (the itch)
Schistosomiasis
Vincent's infection (Vincent's angina, ulcerative or necrotic stomatitis, trench mouth)
Yaws (frambesia)

DISEASES OF CONCERN TO HEALTH OFFICERS BECAUSE OF THEIR GROUP OR EPIDEMIC OCCURRENCE AND THE PRACTICABILITY OF THEIR PREVENTION, AND FOR THESE REASONS OFTEN INCLUDED AMONG THOSE NOTIFIABLE TO THE HEALTH AUTHORITY, BUT NOT TO BE CONSIDERED COMMUNICABLE

Botulism
Food infections and poisonings
Pellagra

The Subcommittee on Communicable Disease Control of the Committee on Research and Standards of the American Public Health Association has formulated certain definitions (Reprint 1697 from the Public Health Reports, Revised 1950) which may be of great value to the physician in the presence of communicable and infectious diseases

Dissemination of Infection. The progress in dissemination of infection of organisms of disease or their toxins, and the clinical manifestations of the process, are as follows:

1 The organism gains the portal of entry and establishes the focus or locus of infection

2 The infection extends from the focus to adjacent or surrounding structures or regions. Signs of such extension are evident, for instance, lymphangitis, but the infectious process and its manifestations still are limited topographically.

3 The established focus or an extension of the focus persists after the dissemination of the infecting agent or its toxins produces manifestations in other organs or systems or in the body as a whole.

The manifestations of an infectious disease which affects the body as a whole are the result of the dissemination of the infecting agent and its toxins through the hemic and lymphatic systems and occasionally through the nervous system (rabies). Often the infecting agent is overcome by the defensive mechanism of the body, so that persistent disease, bloodstream infection or septicemia does not develop. However, the development of septicemia originates disease of the body as a whole.

BACTEREMIA. Bacteremia is a temporary invasion of the blood by bacteria with or without evidence of a continuance of the infection

The blood is frequently invaded by microorganisms which, under normal conditions, are rapidly removed by phagocytosis by the cells of the reticuloendothelial system. Streptococci, occasionally, may be revealed by blood cultures in rheumatoid arthritis. Likewise streptococci and staphylococci may be present in dental infections after chewing; in as many as two thirds of all who have extraction of teeth under general anesthesia, occasionally after extraction under local anesthesia; and after tonsillectomy In such instances there are no clinical evidences of infection although it is visualized that by this method of dissemination localized infection of the fixed tissues may occur

SEPTICEMIA Septicemia occurs when the immunologic resistance of the blood is broken down by unusual numbers or virulence of microorganisms, which multiply in the blood, with the production of toxins and the signs and symptoms of infection. On some occasions the invading microorganisms are not unusually virulent, but the resistance of the host is very low, so that septicemia develops. Secondary infections of the fixed tissues, and particularly of the lungs, pericardium and central nervous system may ensue if the resistance of the patient is low or if the virulence of the invading bacteria is high

The terms bacteremia and septicemia, however, commonly are employed synonymously because it is frequently difficult to draw a sharp distinction between them For example, the occurrence of positive results on blood cultures in the early stage of typhoid fever may be only a bacteremia, since it is usually temporary and occurs at a time when the patient is not severely ill, but if it persists, or becomes more pronounced, it may become an overwhelming septicemia

A true septicemia may be cryptogenic when resistance is low. Furthermore, it may develop very rapidly after an initial infection of a mucous membrane and particularly of the respiratory tract as, for example, the septicemias in the early stages of meningococcal meningitis and pneumococcal pneumonia

The pyogenic bacteria, especially streptococci, staphylococci, pneumococci and meningococci, are the ones most likely to produce septicemia. *Salmonella typhosa, Brucella melitensis, Escherichia coli, Salmonella choleraesuis, Bacillus anthracis, Streptobacillus moniliformis, Actinomyces necrophorus* and the gonococcus less commonly cause septicemia The toxin-producing bacilli, like *Corynebacterium diphtheriae* and *Clostridium tetani* and other clostridia are rarely present in the blood, except *Clostridium perfringens Escherichia coli, Pseudomonas aeruginosa, Alcaligenes faecalis, Hemophilus influenzae, Klebsiella pneumoniae* and the bacteroides rarely multiply in the blood

Septicemia, a general infection resulting from what was originally a local process, may originate from a recognizable focus of infection, as unclean traumatic wounds, puerperal sepsis, pneumonia, gonorrhea, and typhoid fever. In the majority of such cases septicemia is due to the streptococcus or the staphylococcus, but there often are combined or mixed infections; that is, the septicemia may be

caused by the simultaneous presence of the *Streptococcus pyogenes* and the *Salmonella typhosa*, the *Diplococcus pneumoniae*, or the Klebs-Löffler bacillus.

In other cases the focus of infection is not recognizable during life (cryptogenic septicemia) and perhaps not at necropsy. Generally, in these cases of unrecognizable focus, the patient is already ill of some malady, acute or chronic, but in a certain proportion the infection occurs in persons who are in good health

A streptococcal septicemia often occurs during the course of a local or a general infection as a secondary or an intercurrent event in chronic diseases, especially in arteriosclerosis, cirrhosis of the liver, Hodgkin's disease, leukemia, and the chronic forms of nephritis, valvular heart disease, and tuberculosis and other maladies. Because of the fact that these infections are likely to close the scene, they are spoken of as terminal.

When septicemia starts from a local infective focus, the symptoms of the invasion may begin immediately At the onset there is usually chilliness rather than rigor, with fever, moderate at first, but which rises and tends to become of the continued type, with decided daily remissions. There are headache, anorexia, prostration and perhaps delirium. The pulse is rapid, small, and compressible. The tongue shows a marginal redness, and may become dry and brown, evidence of dehydration from the fever There may be nausea, vomiting, and diarrhea, and the spleen may be palpably swollen Petechial spots in the skin and mucous membranes are common, slight jaundice often develops; and scarlatiniform rashes and complicating infection by the groups of herpes simplex viruses may appear on the lips and in the mouth The urine frequently contains albumin, leukocytes, erythrocytes, and tube casts. If the septicemia is cryptogenic, and especially if it is due to the presence of the streptococcus, the fever is high and irregular, and there are recurrent slight chills.

Septicemias are prone to cause localized disease in some region, organ or system of the body. The common sites for the localization of disease from the presence of circulating germs in the blood include the endocardium, especially the valves of the heart, and the pleural, pericardial and peritoneal cavities. The central nervous system likewise is often affected, meningitis or abscesses originating within the organs of this system. The organ of special sense most commonly affected by streptococcal infection is the eighth cranial nerve. Otitis media affecting the special sense organs of hearing is one of the commonest causes of deafness. Conjunctivitis is exceedingly common.

Septicopyemia The presence of septicemia is evidence that the defensive mechanism of the host has been overcome and that pathogenic bacteria have entered the circulatory system from a focus of infection and have established a habitat within the blood stream The term septicopyemia derives its meaning from the fact that it indicates a combination of pyemia and septicemia Differentiation of septicemia from septicopyemia rests on bacterial invasion of the body as a whole. In septicopyemia the bacteria are fed into the blood stream by means of the intermittent breaking off and casting into the circulation of vegetations containing the bacteria. Blood cultures in septicemia are consistently positive, whereas in septicopyemia they may be intermittently positive. Septicemia may develop during the course of many infections, but streptococcal infections are the commonest of all. The most known example is bacterial endocarditis.

THE STREPTOCOCCAL INFECTIONS

The streptococci belong to the family Lactobacteriaceae, tribe Streptococceae, genus *Streptococcus*, type species *Streptococcus pyogenes* The versatility of these organisms as disease agents and their extensive distribution in both man and animals render them potent agents of disease.

On the basis of the Lancefield group-specific and type-specific substances, the streptococci are arranged alphabetically in defined groups from A to I, and the bacteria in each group are further divided into types which are numbered 1, 2, 3, 4 and so on. In group A, 60 or more types are listed

The *epidemiology* of streptococcal infections involves a host-parasite relationship and the environment in which the host-parasite relationship is maintained. The spread of streptococcal infections exemplifies air-borne infections.

In the tropics the hot climate at low altitudes does not favor development of streptococcal infections Ascent from the low levels to the high levels reveals a steadily increasing morbidity rate for streptococcal diseases. The relation of temperature to the morbidity rate of scarlet fever, for example, is illustrated by the seasonal incidence of this disease and other streptococcal infections in temperate climates.

The type distribution of streptococci is cosmopolitan In an extensive study of air-borne diseases during the recent war, streptococci from twenty-two countries were collected simultaneously and typed It was found that every type of streptococci was represented in each country In every locale, at any given time, the existing streptococcal diseases are produced by the types of pathogenic streptococci that are predominantly present, while in that same locale other types of streptococci may be present but not actively producing disease This situation is not static. A particular type of streptococcus may induce scarlet fever for a long time It then may lose the ability to produce the erythrogenic toxin that seems to be characteristic of the disease and become inactive as a producer of scarlet fever without, however, any decrease in its virulence as a producer of other streptococcal diseases Different types of streptococci may simultaneously cause the same disease independently of each other For instance, in a given community a streptococcus of one type may have been producing sporadic cases of scarlet fever, when suddenly the disease assumes epidemic form and it is found that the epidemic cases are caused by another type of streptococcus. When the epidemic has passed, sporadic cases of scarlet fever due to the first type of streptococci again occur A second epidemic of *scarlet fever may now be initiated by an increase in the number of sporadic cases* The kinds of streptococcal diseases in any locality are constantly varying, not because of altering environmental conditions but because of changes within the streptococci themselves.

There is a seasonal variation in carrier rate that parallels the morbidity rate of streptococcal disease

Carriers are more dangerous in the spread of streptococcal diseases than are persons acutely ill from the diseases, since the sick do not get around A carrier disseminates a disease by exhaling air-borne bacteria which are transmitted to nearby persons by direct inhalation or by indirect or delayed inhalation after the carrier has gone, by handshaking or by handling articles and food The spread of streptococcal disease through foods or drink (milk) is slow compared with air-borne spread by an active carrier

The streptococcus produces a variety of toxic products, endotoxins, exotoxins, hemolysin, erythrogenic toxin, leukocidin and fibrolytic substances. In response to these products the host reacts by developing all of the ordinary immunologic reactions An infection by a streptococcus confers a kind of immunity for indefinite periods.

The streptococcus seems to be susceptible in a semispecific manner to the bacteriophage

It is agreed that the streptococcus group A of Lancefield, containing the subgroups 1 to 60 or more, causes the greater part of the *streptococcal diseases* In occasional instances other groups, for instance, groups B and C, may be etiologic agents.

As a rule during a localized infection by a streptococcus the host resistance does not permit establishment of another locus elsewhere in the body. *During the* time a virulent species of infecting streptococcus is circulating in the blood stream, however, if there is not a sufficient defensive force, that is, if the host resistance is not strong enough, the organisms establish themselves in other organs or structures of the body.

The complications of streptococcal disease are in reality progressions of the

original acute focal infections, and they may involve all the topographic or systemic divisions of the body.

In the *integumentary system* streptococcal involvement is by localization in the skin, subcutaneous areolar tissues or mucous membranes in parts of the body distant from the original focus, as cellulitis, that is, Ludwig's angina; in the breast, especially the lactating breast, as mastitis and breast abscess.

In the bones and joint structures the streptococcus causes acute suppurative disease of joints, osteomyelitis, bursitis, abscess of muscle, tenosynovitis and other acute pyogenic processes of this system.

In the *respiratory system* the streptococcus may localize in the nasal accessory sinuses, causing sinusitis, or in the lungs, originating pneumonia The pneumonias produced by streptococci usually are of bronchopneumonic distribution and manifestations Pulmonary abscess without pneumonia may occur. After epidemics of the exanthems, especially measles, secondary streptococcal pneumonia as a complication is to be expected Terminal and streptococcal pneumonia and septicemia frequently occur during postoperative convalescence and in the aged

In the *cardiovascular system* localization of streptococci, producing pyogenic endocarditis and pericarditis, in a heart already injured by disease or by congenital defect, is not unusual. The *venous* division of the cardiovascular system frequently is involved and the involvement is manifested by acute phlebitis, which may proceed to abscess formation In all of these streptococcal infections there is tachycardia The pulse rate is out of proportion to the degree of fever, even though the heart is not affected

In any of the manifestations of the streptococcal state, whether the infection is limited to the original focus or has extended and set up a focus or foci in other regions of the body, the cellular elements of the blood are disturbed A polymorphonuclear leukocytosis is present except when a virulent strain of the streptococcus quickly overwhelms the resistance of a person who was in good health prior to the infection, or in a person seriously debilitated owing to any cause prior to the infection In each of these instances there is little or no increase in the number of leukocytes. In an occasional patient when resistance is overcome there is definite leukopenia. An unusual but significant exception to the rule that there generally is leukocytosis by polymorphonuclear leukocytes is the occasional accompanying eosinophilia Eosinophilia may indicate that there has been previous circulation of a similar antigen

Direct extension of streptococcal infection from the primary focus, usually in the skin, is first through the *lymphatic system* or the circulatory system. Extension through lymphatic channels is manifested by enlargement of lymph nodes and by lymphangitis, reddened streaks radiating from the original focus Cellulitis and abscess formation may be primary in the original focus or secondary to it Cervical adenitis accompanies many of the acute infections by the streptococcus.

In the *digestive system* occasionally a blood-borne streptococcal appendicitis occurs. Reflex digestive symptoms of anorexia and vomiting, however, are common manifestations of most of the acute streptococcal infections The accessory digestive glands may be affected The parotid, the submaxillary or the sublingual glands may be affected These infections usually resolve but may terminate in abscess formation Acute inflammation of the ducts attends these infections The incidence of cholangitis and jaundice is low and is difficult to determine; that of pancreatitis is even lower. Streptococci ingested in contaminated food are likely to result in epidemics of sore throat or tonsillitis, but rarely in gastroenteritis, since these bacteria, unlike the staphylococci, do not cause a specific form of food poisoning.

In the acute streptococcal infections considered thus far, the portal of entry of the streptococcus is through the oral or the nasal cavities or the skin, and the infections involve the urogenital system seldom and only secondarily.

The possibility of the primary entrance of the streptococcus through the orifices of the *urogenital system* is real. Of the primary ascending streptococcal infections, the commonest is pyelonephritis. Occasionally acute cystitis, pyelonephritis or perirenal abscesses may be hematogenous in origin. Streptococcal infections may occur locally or generally after instrumentation of the urinary tract, the organisms establishing themselves at a point of injury or entering directly the lymphatic and circulatory systems That these infections may occur from the same groups and types of organisms that produce scarlet fever in the usual way is evidenced by such connotations as puerperal scarlet fever. Along with other pyrogens the streptococcus is a prominent etiologic agent in the production of puerperal or childbed fever. Acute glomerulonephritis, often associated with scarlet fever, does not result from localization of the streptococci in the kidneys.

The *endocrine system* usually escapes the acute streptococcal infections.

Localization of the streptococcus in the *central nervous system* may occur during an acute streptococcal infection from any portal of entry. Unless the organism enters during surgical operation or through traumatic wounds, streptococcal infections of the central nervous system are always borne by the blood stream. The common manifestation is acute purulent meningitis. Brain abscess also occurs. Either of these diseases may come on after an infection in the skin or in an orifice of the body that may have been too mild to attract the attention of the patient.

Scarlet Fever. SYMPTOMS. Scarlet fever is caused by an erythrogenic streptococcus

The incubation period of scarlet fever is uncertain, from 1 day to 7 days, sometimes 11 days or longer The onset of symptoms likewise is exceedingly variable. In many instances the onset is abrupt, with vomiting and fever The temperature rises abruptly and may reach 103 to 105 F (39.4 to 40.5 C), reaching a fastigium on the second day and slowly receding during the following week.

There are chilly sensations, but rarely is there a chill. The pulse from the beginning is fast, out of proportion to the rise in temperature.

The disease may begin as a sore throat, or the manifestations may begin with suddenness and severity, with hyperpyrexia, delirium and prostration.

EXAMINATION. On examination it is observed that synchronously with establishment of the height of the fever the rash appears, first on the neck and thorax, whence it may remain localized or spread over the whole body within the next 24 hours. After 2 to 4 days the rash disappears or begins to fade rapidly. The developing rash of the tongue and the subsequent lingual desquamation have been given suggestive titles, "strawberry tongue" and "raspberry tongue." The papillae of the tongue are reddened and swollen During the height of the rash the skin from a distance appears uniformly and brilliantly scarlet, but on examination the eruption is observed to consist of fine, closely set red points on a diffusely reddened background. A transient blanching of the rash is produced by pressure on the skin The cutaneous manifestations in scarlet fever may be atypical or lacking Sometimes punctate rashes occur, either alone or with the general rash, distributed irregularly over various regions of the body. The mucous membrane of the mouth and throat is brilliantly and deeply erythematous; the tonsils are diffusely reddened.

When the fever subsides, desquamation begins, usually proceeding in the regional order in which the rash appeared. Complete desquamation, which includes the tongue and the mucous membrane of the mouth may occur and if so, it is a slow process requiring from 1 to 2 months The cuticle usually separates in small scales, but it often can be peeled away in large flakes.

In severe scarlet fever the rash may be irregularly distributed and hemorrhagic, and each day it may become darker in color. Clear vesicles develop and become turbid as time passes. The entire skin may be covered, with small yellow vesicles

on a red background (scarlatina miliaris) Widespread purpuric eruptions may appear at the onset of symptoms or may attend desquamation. Ecchymosis in dependent parts such as the scrotum may occur.

The leukocyte count is from 15,000 to 40,000 per cubic millimeter of blood, indicative of the response to the invading organisms. The spleen may be enlarged, but the enlargement is not diagnostic. Urinary changes are significant of dehydration and fever or of cloudy swelling of the kidneys.

DIAGNOSIS. The diagnosis of scarlet fever usually can be made by the sudden onset of high fever, vomiting, extraordinarily rapid pulse, the reddened swollen papillae of the tongue, and the early appearance of the rash. Throat cultures reveal the presence of a hemolytic streptococcus

Acute follicular tonsillitis may run a clinical course indistinguishable from that of scarlet fever, especially when scarlet fever does not present a cutaneous rash or when it is accompanied by an atypical rash.

Diphtheria may be accompanied by a cutaneous eruption over the thorax. This eruption is not so brightly colored as that observed in scarlet fever. In any event, the diagnosis of either scarlet fever or diphtheria is not based on the appearance of the cutaneous eruption Cultures from the throat grown on appropriate mediums will enable one to make the proper differentiation

Rubella is attended by a cutaneous eruption resembling that of scarlet fever, except that the rash in rubella is not punctiform. When rubella is suspected, the patient should be isolated and kept strictly away from pregnant women, since rubella during pregnancy may cause malformations of the fetus.

The Dick test determines susceptibility to scarlet fever The test is carried out after a preparation of the toxin has been made so that the skin test dose of the toxin is contained in 0.1 ml. of the preparation. The dose is injected intradermally into the flexor surface of the forearm A circular or oval area of erythema 1 cm. in diameter or larger occurring at the site of injection 24 hours after injection indicates that the subject is susceptible to scarlet fever

COMPLICATIONS Otitis media is one of the commonest and most important complications of scarlet fever. The streptococcal focus in scarlet fever is the throat, from which the infection ascends through the eustachian tubes to involve the middle ear. Otitis media may come on at any time during scarlet fever or during convalescence from the fever It is manifested by recurrence or enhancement of fever and by pain in the ear with evidence of increased tension on the membrana tympani unilaterally or bilaterally Williams pointed out that 10 8 per cent of otitis media and 1.1 per cent (15,733 cases) of mastoiditis and sinusitis of accessory sinuses are complications of scarlet fever Thrombosis of the lateral sinuses, meningitis and brain abscess may result from otitis media Paralysis of the facial nerve may result from bone necrosis incident to middle-ear disease

In the second or third week or later, glomerulonephritis often arises as a sequel of any one of the acute streptococcal diseases, but often from scarlet fever. Acute glomerulonephritis is manifested by edema and the presence of erythrocytes and tubular casts in the urine. Usually in the streptococcal infections the urine remains essentially negative during the course of the disease except for small amounts of albumin, not more than grade 1 (on a basis of 1 to 4, grade 1 being the least amount) Mild forms of glomerular involvement, glomerulitis, may occur and may do great injury to the kidneys, injury which may not be manifested until months or even years later and then as chronic glomerulonephritis If nephritis occurs recovery is to be expected in most instances Rapidly progressive nephritis, however, is accompanied by hyperazotemia and edema of the glottis and is followed immediately by generalized edema. The mortality rate in these rapidly developing nephritides may be high.

Acute follicular tonsillitis, epidemic streptococcal sore throat, and phlegmonous

or suppurative tonsillitis are all streptococcal infections by strains of the strep
coccus which are not at the time producing an erythrogenic toxin.

Ludwig's Angina. Ludwig's angina is a rare disease caused by a streptococ
infection, either following a sore throat or occurring secondarily as a complicati
of one of the specific infections, especially diphtheria or scarlet fever. The disea
is characterized by a swelling beginning in the submaxillary region or regions, a
spreading to the floor of the mouth and the front of the neck. There are fever a
much pain, with dysphagia and difficult mastication and articulation. Grave dyspn
may supervene from compression of the larynx or edema of the glottis.

Erysipelas. SYMPTOMS Erysipelas is a streptococcal infection. The incubati
period varies from 3 to 7 days. The disease commences with a chill or chilline
followed by a rise of temperature to 103 to 105 F (39.4 to 40 5 C). In previous
strong and healthy persons the constitutional depression may be slight, but in t
old or debilitated, or in chronic alcoholics, there may be great prostration, d
tongue, feeble pulse and delirium

EXAMINATION. In an erysipelas not secondary to surgical operation or injur
on examination a reddened spot is observed, usually on the bridge of the nose
on one of the alae, occasionally on other parts of the face, on the ear, or on t
scalp The spot becomes apparent with the onset of the fever This reddened ar
rapidly enlarges; the skin becomes swollen, erythematous and tense and is ofte
studded with vesicles or small bullae, especially on the eyelids, ears, and forehea
The pain is burning and intense The inflammatory area has a well-defined, som
what raised margin, and as it extends, the areas first attacked become somewh
lighter in color and less swollen than earlier in the disease. When the greater portio
of the face is involved, the eyes are swollen shut, the nose is bulbous, the lips an
ears are thickened and edematous The cervical lymph nodes are enlarged. Sma
cutaneous abscesses are common on the neck, cheeks, and forehead, and there ma
be extensive suppuration under the scalp The mucous membrane of the mouth an
throat is reddened, and in rare cases the inflammation may extend to the laryn
and cause edema Leukocytosis is present, and the urine is often albuminous.

DIAGNOSIS The diagnosis is based on the clinical findings and is supported b
positive cultures of virulent streptococci from wounds or from the throat.

COMPLICATIONS AND SEQUELAE Septicemia, pyemia, ulcerative endocarditis
peritonitis, meningitis, and articular rheumatism are relatively frequent complica
tions of erysipelas. Pericarditis, pleurisy, acute nephritis, pneumonia and otiti
media occur less frequently Despite meningeal symptoms such as delirium, coma
and meningismus, meningitis is rare

Puerperal Infection. Puerperal infection by the streptococcus is one of the
most serious diseases produced by this organism

The common lesion of puerperal fever is *endometritis* Three or 4 days afte
delivery the patient suddenly experiences malaise and complains of headache and
a feeling of chilliness, or she may have a well-defined chill, the temperature rising
to 103 F (39 4 C) or higher Generally only one chill occurs, after which the tem-
perature remains constantly elevated. The pulse becomes extremely rapid, and
later it is weak and of small volume

The endometritic implication is slight The lochia is thin and not profuse The
patient may complain of intense pain, which is at first limited to the lower portion
of the abdomen but gradually extends over the entire abdomen At the same time
there is marked tympanites, and the abdominal walls are rendered tense by the
distended intestines. If a fatal issue ensues, death usually occurs within 10 days
after delivery, the patient gradually failing In other cases, however, the clinical
symptoms do not correspond to the gravity of the lesion, the temperature is but a
little elevated, the pain slight, and the abdominal symptoms are slight or even

absent, the serious character of the condition being indicated only by the rapid and compressible pulse and the drawn and haggard facies.

In cases of postpartum *pyemia* the symptoms are characteristic. The initial chill occurs by the end of the first week, and the temperature does not remain constantly elevated, but instead there are an intermittent fever and chill, with remission, recurring in succession The symptoms vary considerably, according as the cause is the dislodgment of a single thrombus or is the repeated entry into the blood of small infected particulate matter. In the first event a metastatic abscess develops at some one point, the symptoms depending on the organ involved. In the second event, if thrombi are being constantly dislodged, there may be symptoms referable to various organs

One of the most constant manifestations of postpartum pyemia is bronchopneumonia which contributes to the fatal termination. In other instances swellings at the various joints occur in association with the pneumonia or without it. Suppuration of the joints may lead to total destruction of the joint tissues. Abscesses also may develop in the internal organs or appear on the surface. They may occur in the eye and may lead to its destruction. The course of pyema varies according to the organs attacked and the resisting powers of the patient, and weeks, or sometimes months, elapse before death occurs or recovery ensues

In rare instances the infection is so virulent that the bacteria do not have a chance to become localized in any one organ, and both they and their toxins are found in abundance in the circulating blood, with very slight implication of the uterus. This results in the so-called *acute septicemia—sepsis foudroyante*—which represents a most rapidly fatal form of infection, the patient occasionally dying on the second or third day after delivery in a condition of shock, and without the development of local symptoms Streptococcal septicemia in the postpartum patient has been known to end fatally within 18 hours after the initial rise of temperature.

Occasionally the thrombotic process involving the pelvic veins may extend to the femoral vein, and sometimes to the saphenous vein, on one side or both sides, giving rise to *phlegmasia alba dolens*

EXAMINATION. On examination there is some tenderness in the lower part of the abdomen, and the uterus is larger and more doughy in consistency than normal The lochial discharge is sometimes increased in quantity, is partly bloody, partly purulent in character, and may be practically devoid of odor In severe streptococcal puerperal infection, when the fever is high, there may be very little lochia

DIAGNOSIS The diagnosis of streptococcal puerperal infection is usually established by the history, the examination and the character of the lochia if any be present. The diagnosis of pelvic or generalized peritonitis is based on physical examination and symptoms. The diagnosis of pyemia and septicemia is established by blood culture

As has been stated, the commonest puerperal infection is some form of endometritis, and the differential diagnosis comprises a decision whether the presenting variety is septic, putrid, or gonorrheal Cultures of the lochia often reveal the causative organism

Streptococcal Infections Produced by Miscellaneous Aerobic Streptococci. Aerobic streptococci are separable into four divisions hemolytic streptococci, entero- [illegible]

[illegible] grown on blood agar plates, but a competent bacteriologist can distinguish the differences between these streptococci and the pathogens

Chronic Focal Streptococcal Infections. In the British Museum is preserved large collection of clay tablets, which at one time constituted a part of the library of Ki Ashurbanipal, of Assyria, of the Sargonid dynasty (668-626 B C.). In one of the lett of the Court physician to his king, a most remarkable diagnosis of a dental ailment h been described... Unfortunately we shall never know the name of the physician w wrote it, as the tablet is broken and the fragment which would have contained the supe scription is lost... The physician writes to the king saying "The inflammation whe with his head, his hands (arms), feet (legs), are inflamed, is due to his teeth. His tee must be drawn it is on this account that he is inflamed, he will reduce (it(?)) throu internal (channels) (?). Then will all be well" (The foregoing quotation is from the It Journal; for the source of this translation we are indebted to C. J Gadd, Keeper of t Museum)

Since this centuries-old communication, clinical experience has proved abu dantly that serious diseases may arise from a chronic focus of infection. In ma instances the infecting organisms have been traced from their focus, for instanc the throat, to tissues in remote parts of the body In such cases the causative rel tion is a proved fact The difficulty in the practice of the theory was recognized l Frank Billings and his students, Ernest E Irons and Edward C. Rosenow, wl subsequently originated and sponsored much work on chronic foci of infection This difficulty is the laborious and complicated problem of determining the exa nature of the relationship between a focus of infection and, let us say, chron arthritis, and often the task is insurmountable

The desirability of finding and removing local and often symptomless infectio is generally recognized However, the removal of teeth and tonsils, operations o the nose and nasal accessory sinuses, treating or cauterizing a cystic cervix, an massaging the prostate on the chance of possible relationship between infection an the bizarre complaints of neurotic persons are not scientific procedures. The remova of definite chronic alveolar infections and definitely infected tonsils, however, shoul be done as treatment for local conditions Promises of relief from chronic existin diseases, or of benefit from treatment, should not be given

The diagnosis of a chronic focus of infection as the cause of systemic diseas usually cannot be made until the focus has been removed and until clinical progres of the disease indicates that the focus was the causative factor in its production.

The *Streptococcus viridans*, or green-producing streptococcus, generally is a harmless saprophyte Some varieties of the streptococcus, however, are pathogen since they produce abscesses at the roots of the teeth, sinusitis, and disease of th middle ear These latter organisms, therefore, are prominent in the theory of chroni focal infections because the focus, according to this theory, often is symptomless Many allergic and toxic disorders, due to long-continued growth of bacteria in th bodily tissues, are attributed to the presence of these organisms.

The definite and important disease produced by the *Streptococcus viridans* is *subacute bacterial endocarditis*. During febrile periods of the disease the organisms can be cultured from the blood stream In this disease there almost always has been some sort of predisposing injury or deformity of the heart or its valves prior to the establishment of the growth of the bacteria on the cardiac valves, for example, an ancient rheumatic fever or a congenital defect Previous to inauguration of antibiotic therapy, prognosis in this condition was almost invariably hopeless

In recent years another streptococcus has been observed which has been designated as "S. B E.," simply indicating that the organism causes serious if not always fatal streptococcal endocarditis So far as has been stated, this organism does not participate in chronic foci of infection

THE STAPHYLOCOCCAL (MICROCOCCAL) INFECTIONS

The staphylococci belong to the family Micrococcaceae, genus *Micrococcus*, and species *Micrococcus pyogenes* var. *albus* and var. *aureus*, and *Micrococcus citreus*.

In warm climates, or during the warm seasons in the temperate zones, staphylococcal infections are commoner than elsewhere or in cold weather, and predominantly affect manual workers, who are subjected to trauma to the skin, as by sweaty clothing, or by other dermal irritants such as heat, wetness, dusts or particulate matter. Cutaneous wounds and the accompanying traumatized tissues afford a favorable field for the infection. Debilitated persons, young or old, during convalescence from fevers are particularly subject to staphylococcal infections. The presence of hyperglycemia or azotemia or both furthers the bacterial action. Some persons have allergic cutaneous reactions due to staphylococcal infections.

The diseases produced by the staphylococcus, *Staphylococcus aureus* in particular, may be manifested in any of the chief topographic areas or systems of the body. These diseases are considered in their appropriate places in this text.

Diseases due to staphylococci occur sporadically, endemically and epidemically.

The staphylococci, which in man are parasitic on the skin and in the mucous membrane of the bodily orifices, live in commensalism with other bacteria. Williams, Miles and associates observed that the nasal occurrence rate for *Staphylococcus aureus* among people of the working class who came to the hospital for the first time fluctuated between 19 and 65 per cent during the period from October to July. The mean rate, 47.4, agreed with the carrier rates that had in the past been determined mainly in hospital patients and personnel. The persons studied consisted of three groups. (1) outpatients attending the hospital for the first time with recently inflicted wounds, (2) male inpatients, in a ward, with established wound sepsis and (3) the nursing staff of the same ward The outpatients studied had a gross nasal carrier rate of 47.4 per cent and a wrist carrier rate of 18 4 per cent. The nasal carrier rate of the inpatients studied, calculated from their admission swabs, was 49 4 per cent. The nasal carrier rate among the nurses was significantly higher than for the newly admitted patients. The authors expressed the belief that carriage or noncarriage of staphylococci therefore appears to be a more or less persistent phenomenon. There appears to be a relationship between the carriage of staphylococci in the nose and on the skin.

From the study of Williams and Miles of infection and sepsis in industrial wounds of the hand they concluded that the incidence of *Staphylococcus aureus* contamination of small wounds of hands cultured within 6 hours after infliction was about 20 per cent; the positive incidence of cultures for *Streptococcus pyogenes* was 1 to 2 per cent Staphylococcal wound contamination was commoner in skin carriers of a staphylococcus which was of the same phage type as the one isolated from the wound Sixty per cent of the staphylococci isolated from wounds were derived from the patient's own skin, and no infections were derived from the wounding agents. Self-infection of this sort is rare in streptococcal infections.

Severe wound infections of the hand which ended in a general sepsis were almost always staphylococcal in origin and never due to simple streptococcal infections. About half of the staphylococcal and one fourth of the streptococcal infections were introduced into the wounds However, the streptococci so introduced, in contrast to the staphylococci, which are in 60 per cent of the cases from the patient's own skin, are from sources extrinsic to the patient.

Of the possible factors which predispose to infection and sepsis only staphylococcal skin carriage and wound contamination by staphylococci could be shown to have a constant effect.

The bacterial flora of accidental wounds is a complex mixture of bacteria. Rustigian and Cipriani delineated the characteristic flora of wounds as often being composed of *beta hemolytic streptococci*, *Staphylococcus aureus* and *Staphylococcus albus*, enteric streptococci, *Clostridium*, *Proteus*, *Pseudomonas* and coliform bacteria.

Staphylococcal Food Poisoning. The sickness which follows ingestion of food containing living viral or bacterial agents which are capable of producing infection is *food infection*. Food infection is distinguished from food poisoning. *Food poisoning* may result from dead bacteria or their toxins, chemical agents, plant products and other miscellaneous poisons contained in the food. Etiologically, food poisoning is diagnosed by laboratory methods.

The history of a patient ill with food poisoning should contain the following information: the first symptoms observed by the patient, and the time of the appearance of each successive symptom; the presence or absence of pain, vomiting, diarrhea and constipation; an itemization of all food eaten during the preceding thirty hours, the number of persons who ate the same food, the number who became ill, and the effect on any animals which were fed remnants of food during this time Any food which has not been consumed is examined for abnormalities of appearance, odor, or taste and any such abnormalities are recorded. An aliquot of food, specimens of vomitus and feces are submitted for laboratory examination if this is deemed necessary Extensive examination of food is made only when the health and welfare of the community as a whole are endangered Small epidemics such as may follow the eating of a custard-filled cake at a church dinner are not investigated

It is probable that staphylococcal food poisoning is the commonest type of bacterial food poisoning The poisoning is produced by the enterotoxin elaborated by the staphylococcus The enterotoxin is present in food before it is eaten The other toxins elaborated by staphylococci are lethal toxin, hemolysin, and dermonecrotic toxin

Dack has summarized the factors which are concerned in the production of enterotoxin by staphylococci as follows. (1) the number of organisms, (2) the number of organisms of other types in the food which may overgrow the staphylococci or cause such spoilage as to prevent the food from being eaten, (3) the nature of the food which is infected, and (4) the temperature at which the infected food is kept In temperatures of 16 to 46 C (60 8 to 114 8 F), from 4 to 8 hours are required for the staphylococcus to elaborate enterotoxin, the exact length of time depending on the perishability of the food

The enterotoxin is resistant to cold, and very resistant to heat, although it gradually loses its potency when exposed to high temperatures.

The chief vehicles for staphylococcal food poisoning are cream-filled bakery goods, cheese, doughnuts, milk, ice cream, meat and meat sandwiches. Staphylococci are ubiquitous and are present on the skin, in the respiratory passages and in the air and consequently food may easily become contaminated Persons who have coryza or those with infected abrasions of the hands should not handle food.

The onset of symptoms occurs in 1 to 6 hours after the ingestion of the contaminated food. Salivation associated with nausea is followed promptly by vomiting, retching, abdominal cramps, and diarrhea After the patient vomits there is relief for a time, but vomiting soon recurs The vomitus may contain blood. In some patients, vomiting or diarrhea may be the only symptom The diarrhea may begin with a soft stool which is later followed by profuse watery stools; the latter may subsequently contain blood The severity of the attack varies There may be headache, muscular cramps, and sweating. A period of anorexia may follow the acute attack and may be accompanied by less frequent bouts of nausea, vomiting and diarrhea lasting from 1 to 3 or 4 hours.

Examination, in mild instances of food poisoning, reveals no definite abnormalities attributable to the poisoning. The toxic condition is purely symptomatic.

In severe cases, prostration and dehydration may be marked and fever or subnormal temperature may be present

Symptoms of food poisoning coming on about 4 hours after ingestion of dairy products, meat or cheese sandwiches usually are due to staphylococcal toxins The diagnosis of staphylococcal food poisoning is justified

Laboratory diagnosis involves detailed bacteriologic procedures which consist, first, of culturing the staphylococcus and second, of proving that the particular type of staphylococcus produces an enterotoxin. Not all staphylococci are producers of enterotoxin Generally, the pathogenic strains are highly pigmented and hemolytic.

Complete recovery is the rule An occasional death has been reported. Recovery is usually prompt and occurs in from 1 to 5 days.

Staphylococcal Enteritis (*Hemolytic Staphylococcus aureus, Coagulase Positive*). The importance of staphylococcus as an etiologic agent in severe enteritis is not known. Finland has recently recorded that patients who have been receiving aureomycin or terramycin may develop diarrhea, and that shock and death may ensue. It is presumed that the intestinal flora has been destroyed by the antibiotic with a subsequent overgrowth of the *Micrococcus pyogenes* or staphylococci

PNEUMOCOCCAL SEPTICEMIAS AND EXTRAPULMONARY INFECTIONS

The pneumococci belong to the family Lactobacteriaceae, tribe Streptococceae, genus *Diplococcus*, and species *Diplococcus pneumoniae*. The pneumococcus has a capsule, stains readily with all the usual aqueous aniline dyes, and is gram-positive.

Dochez and Gillespie divided certain pneumococci into types I, II and III and relegated all other pneumococci to type IV. In 1932 Cooper and her associates identified and reclassified 29 types of these previously considered as group IV. However, more recent studies have revealed criteria for division of pneumococci into 75 types

The pneumococcal diseases probably develop on the general plan followed by other pyogenic coccal infections, that is, the infection is disseminated from an acute or a chronic focus in the nose or throat, with subsequent spread by way of the lymphatic channels and the blood vessels and establishment of some other locus in the body From the secondary focus, which is often the lungs, the infection gives rise to severe manifestations, such as acute arthritis, sinusitis, otitis media, mastoiditis, empyema, carditis, peritonitis, meningitis or ulcerative conditions of the eyes. Any of these infectious diseases, especially if it apparently is of spontaneous occurrence in a child, requires consideration of the pneumococcus as the etiologic agent.

During the course of pneumococcic pneumonia, any of the foregoing diseases may set in as a complication In addition there may be formation of abscess at the site of hypodermic injection or in the muscles over the lower part of the thorax and upper part of the abdomen, or in both places Localization of pneumococci in the muscles, with subsequent formation of abscess, occurs probably in hemorrhagic regions of muscles The hemorrhages into the muscles are secondary to coughing.

Endocarditis and *meningitis* may occur together or separately during the course of pneumonia An endocarditis usually is superimposed on rough arteriosclerotic valves or on valves already affected by rheumatic fever. If, during the course of pneumonia, there is a sudden appearance of a diastolic murmur, it should suggest a possible complicating endocarditis If there is a cardiac murmur which changes in quality during the course of pneumonia, the presence of endocarditis should be suspected The definite manifestations of endocarditis are embolic phenomena. During the course of pneumonia the occurrence of meningitis may be the first indication of endocarditis, the meningitis resulting from infected thrombi from the heart. A statement concerning the frequency of this complication cannot be made The meningitis usually comes on at the height of the fever during the course of pneumonia In the majority of cases the meningitis is not distinctly manifested unless the

base of the brain is involved, and this is not common. In any event, when meningitis attends pneumonia, the prognosis is exceedingly bad.

Peritonitis is a rare complication in lobar pneumonia. Peritonitis may begin synchronously with involvement of the pleura in pneumonia or it may extend from the thorax through the diaphragm into the upper portion of the abdomen. Pneumococcic peritonitis independent of pneumonia occurs more frequently in children than in adult patients. Peritonitis may develop during the course of severe pneumonia, but often it cannot be recognized.

Jaundice during the course of pneumonia occurs rather frequently during some epidemics. It seems that jaundice is commoner among Negroes than among whites. Jaundice that develops during the course of lobar pneumonia should not be considered as an exceedingly unfavorable complication.

Parotitis, nephritis and *arthritis* have all been proved to be complications of pneumococcal infections.

A pneumococcal septicemia may be manifested as an atypical pneumonia. Atypical pneumonia in the aged, in adult persons debilitated by chronic disease, and in children may cause a severe illness resembling a septicemia, while infection remains limited to the lungs. Likewise there may be present the manifestations of a septicemia with the disseminating focus in the lungs with minimal manifestations of pneumonia. Almost any infectious illness in the aged and the debilitated that does not conform to definite patterns of disease may be a form of atypical pneumonia with or without extrapulmonary disease.

THE HEMOPHILUS GROUP

The organisms *Hemophilus influenzae*, hemophilus of Koch-Weeks, *Hemophilus parainfluenzae, Hemophilus hemolyticus, Hemophilus suis*, and *Hemophilus haemoglobinophilus* belong to the genus *Hemophilus*, which is a member of the family Parvobacteriaceae.

Various members of the genus *Hemophilus* are important in human infections. *Hemophilus canis* and *Hemophilus ducreyi* affect the genital region and cause soft chancres and chancroids. *Hemophilus pertussis* is associated etiologically with whooping cough. A hemophilic bacillus ("Bacillus X") causes a fatal subacute bacterial endocarditis, the organism is identical with that described in the throats of normal persons.

Hemophilus influenzae. *Hemophilus influenzae*, genus *Hemophilus*, of the family Parvobacteriaceae, is often called also Pfeiffer's bacillus, *Bacillus influenzae* and Koch-Weeks bacillus.

The adult person appears to possess effective resistance to *Hemophilus influenzae*. If the normal defense mechanism be altered, as occurs in severe pandemics of influenza caused by filtrable viruses, a greater prevalence of severe *Hemophilus influenzae* infections in adults is to be expected.

Hemophilus influenzae is regularly found in the respiratory passages in members of families of children in whom this organism has caused meningitis in a brother or sister. Of the adults of the family the mother is the only member who harbors the *Hemophilus influenzae* with any degree of frequency. *Hemophilus influenzae* persists in the nasopharynx for long periods after its elimination from the spinal fluid.

Infection by this organism is not distinctive. It often occurs early as a complication of viral influenza, though this early occurrence is not definite enough to be of value in diagnosis, since pneumonia, streptococcal, staphylococcal, or pneumococcal, can come on early during the course of influenza.

In infection of the respiratory tract a cough may be present which may resemble a whooping cough and may persist for several weeks after the attack has otherwise subsided. Such a cough in adults may be thought to be a second attack of whooping cough.

Hemophilus influenzae may be responsible for an obstructive laryngeal, laryngo-

tracheal or laryngotracheobronchial infection in children 2 years of age or older. The onset is sudden, and the course fulminating. The entire length of acute illness is usually less than 24 hours. During the course of an infection in the upper part of the respiratory tract there is a sore throat Dyspnea starts abruptly and increases within a few hours to such a degree that tracheotomy is imperative. On examination of the pharynx there is diffuse erythema, often with evident edema, and when the tongue is pressed downward, the enlarged red, misshapen, edematous epiglottis is easily seen.

Hemophilus influenzae can produce primary respiratory and extrarespiratory disease. As a primary respiratory disease in most children it produces nasopharyngitis with fever. Many recover from the infection spontaneously. In others sinusitis or otitis media develops. Any portion of the respiratory tract from the epiglottis and surrounding structures to the alveoli may be affected From these foci in the respiratory tract, invasion of the blood may occur. The meninges and joints are sites of predilection for localization. Rarely pericarditis or subcutaneous abscesses result. The severe *Hemophilus influenzae* infections found with greatest frequency are meningitis, obstructive infections of the respiratory tract, pyarthrosis, pneumonia and empyema.

The diagnosis of *Hemophilus influenzae* infections depends on positive cultures of the organism in the body fluids.

In infants and children *Hemophilus influenzae* is a frequent cause of meningitis. The manifestations of influenzal meningitis do not differ from those due to other varieties of bacterial meningitis Therefore etiologic diagnosis depends entirely on a bacteriologic identification *Hemophilus influenzae* pneumonia, empyema, pyarthrosis and other less frequently occurring clinical diseases such as ethmoidal sinusitis with periorbital cellulitis and edema, and pericarditis may occur but they are not solely characteristic of this infection.

The precipitin test can provide immediate diagnosis when organisms are numerous This test can be used for immediate diagnosis of *Hemophilus influenzae* in spinal fluid, in exudate from the middle ear or in a joint exudate, or in empyema fluid.

MALLEOMYCES MALLEI AND GLANDERS AND FARCY

Malleomyces mallei, the causative organism of glanders or farcy, belongs to the genus *Malleomyces*, tribe Pasteurelleae, family Parvobacteriaceae.

When the disease is localized in the nose, it is known as *glanders* The more chronic and constitutional form of glanders, marked by thickening of the superficial lymph vessels, is known as *farcy*. However, both glanders and farcy occur either in acute form or in chronic forms

The essential lesion caused by *Malleomyces mallei* is a granuloma When the lesion begins under the skin, it develops rapidly into formation of abscess, when under the mucous membrane, into ulcers Similar nodules may occur in internal organs

In order that the symptoms of glanders or farcy may be interpreted, a history of association with, or handling of, horses, mules or asses is necessary, because the disease does not occur spontaneously in any other farm animal. The protean manifestations in both the acute and the chronic stages may resemble other diseases

Acute glanders begins with an infection at the site of cutaneous injury with swelling, redness and lymphangitis. There are a high fever, headache, backache and anorexia. From 1 to 4 days later the mucous membrane of the nose becomes involved, ulcers form rapidly, and there is a mucopurulent discharge. Ulcers and abscesses begin to break out over the face and about the joints The nose swells and cutaneous eruptions ensue The lymph nodes of the neck are enlarged, and within a few days the symptoms of pneumonia develop. Whole regions of the subcutaneous tissue may break down and gangrene may follow.

The disease acute farcy is very much like acute glanders except that it is a more

generalized infection with less localization in the nose and about the face. Little is known of the chronic forms of the disease.

On examination the findings depend on the stage of development of the disease The initial lesion in the skin is a nodule at the site of the infection surrounded by a region of lymphangitis and swelling A generalized eruption ensues which may resemble the eruption in smallpox or syphilis The findings as the disease progresses depend on the organs involved. Pneumonia is a constant development

Bacteriologic examination with injection of guinea pigs offers the only dependable diagnostic criterion for these diseases The prognosis is always bad No specific remedy is known In a few instances of the so-called chronic type recovery may have occurred Fortunately, the disease is exceedingly rare and in recent years has become much rarer

Syphilis, tuberculosis, epithelioma and a variety of other diseases, including granuloma inguinale, lymphopathia venereum, chancroid and mycotic lesions, are differentiated by bacteriologic methods, as are typhoid fever, acute rheumatic fever, and general septicemia from any cause.

MALLEOMYCES PSEUDOMALLEI

Melioidosis is a glanders-like disease of rodents, transmissible to man, which occurs in India, the Malay States, and Indo-China Melioidosis is distinct from tularemia, which is caused by *Pasteurella tularensis*, although clinically the two diseases resemble each other closely

THE SALMONELLAE

The enteric group of bacteria (Enterobacteriaceae) includes gram-negative, nonsporulating rods Some (*Salmonella*) are the etiologic agents of gastroenteritis, typhoid fever, paratyphoid and other enteric fevers, and of various types of septicemic infections; others (*Shigella*) cause bacillary dysentery, still others are intestinal saprophytes but may cause pathologic processes in the urogenital and respiratory systems and after wounds or injuries (see pp 965 and 763)

The Salmonellae *Salmonella*, a genus of bacteria of the family, Enterobacteriaceae, comprises gram-negative, nonspore-forming, motile bacilli The different species are closely related antigenically All are usually pathogenic for man or animals

There are three main types of clinical manifestations of salmonella infection, namely, the enteric fevers (typhoid and paratyphoid fevers), gastroenteritis, and a localizing type with foci in one or more organs accompanied by septicemia.

Salmonella typhosa (*Typhoid Fever*) The bacillus of typhoid fever, species *Salmonella typhosa*, genus *Salmonella*, tribe Salmonelleae, family Enterobacteriaceae, is often termed *Bacillus typhosus*, or *Bacillus typhi abdominalis*

Salmonella typhosa has no distinctive physical features that differentiate it from the other species of salmonella It is actively motile, has 12 or more flagella peripherally arranged, it stains readily with the usual aniline dyes, and is gram-negative The final differentiation of the bacillus is best based on specific agglutination

Smooth motile and smooth nonmotile forms contain special antigenic factors called the H factors in the flagella or in the soluble specific substances as do the other species of salmonella An antigenic pattern has been evolved for the four varieties of *Salmonella typhosa*, and their relationships have been established in part Immunization with pure O antigen produces O antibodies; immunization with the motile OH organisms produces both H and O antibodies. The H antigen and antibody apparently have no relation to protection.

The source of typhoid fever is typhoid bacilli living within the bodies of infected persons Infection with typhoid fever means that the infected person has ingested something that was contaminated by the fecal excretion of a typhoid carrier or a typhoid patient.

Generally one attack of typhoid fever protects against a subsequent infection Circulating antibodies disappear from the typhoid convalescent within the first 7 or 8 months after recovery. The permanent immunity is explained as a special endowment of the tissue cells. There are present in the blood serum of the typhoid immune human being bacteriolytic, bactericidal and agglutinating substances, and to a lesser extent precipitating and opsonic bodies.

Agglutination (Widal reaction) is a specific immunologic phenomenon employed in the diagnosis of typhoid fever. The test antigen is a suspension of heat-killed typhoid bacilli. The test is performed by determining by dilution the smallest amount of the patient's serum which can agglutinate the organism If the organisms are agglutinated by the patient's serum, the Widal reaction is positive, and the patient is considered to have typhoid fever if he is ill with a fever which has lasted for at least 10 days or more, and if he has not had the disease within recent years. Exception to this rule is that a patient who has had a prophylactic vaccination against typhoid fever may give a positive Widal reaction. False positive Widal reactions may be present in a patient who has been vaccinated against typhoid and paratyphoid fevers if the test is performed during the course of fever and infection with organisms other than typhoid bacilli (anamnestic reaction).

The interpretation of positive results obtained by the modern Widal reaction is as follows· (1) for O agglutinins, the significant titers, as reported from the laboratory, are those above 1 50 since a few normal persons have titers as high as 1:50 and rarely 1:200 or above, (2) for H agglutinins, titers of 1:80 or above appear to have some diagnostic significance. It is emphasized that the results of these agglutination tests are to be interpreted only with a full knowledge of the history of the patient, especially with reference to previous vaccination against typhoid fever, that the repetition of the test should be made in order to secure an index of the rise or fall of the agglutinin titer, and that only when the titers are high, O 1.500 or H 1:1,000, can they be said to be diagnostically significant The presence of O agglutinins in high titers with H agglutinins absent or present in low titers strongly suggests typhoid fever, even in a previously vaccinated person If there is a high titer of F [illegible]
absent or present in low titer, this suggests
possibly nonspecific stimulation as from a fe
than typhoid fever in a vaccinated person A very high H titer above 1:1,280 may be significant even in vaccinated persons The determination of O and H agglutinins does not serve to distinguish typhoid infection from infections with the closely related members of the enteric group of organisms, especially *Salmonella paratyphi* and *Salmonella schottmuelleri.*

If a polyvalent antigen is employed with proper technic, the complement fixation reaction or test is of high specificity. About one half of patients who have typhoid fever give positive reactions between the first and second weeks of the disease and between 90 to 95 per cent of patients who have typhoid fever give positive reactions after the second week of the disease

Carriers The most important channels of transmission of the typhoid organism from the carrier or the sick person to those who are in good health are, in the following order, drinking water, milk, uncooked vegetables, shellfish, and flies, which may play an important role in carrying of typhoid bacilli from feces to food In recent years, with improved sanitary measures in operation in the sickroom, contact infections become more and more important Contact infection takes place from fomites, fingers, food to mouth, towels, bedclothing and underclothing

As soon as the typhoid bacilli are ingested, they begin to grow in the intestine. During the latter period of the incubation time they begin to appear in the feces After the second week of the disease large numbers of the bacilli are passed *in the stools* Large numbers continue to be discharged in the stools until toward the end of the disease They are continuously discharged in small numbers throughout convalescence, and sometimes for months or years thereafter During the second and *third or later* weeks of the disease the organisms appear in the urine. Unusual routes of discharge of the bacilli from the patient are in pus from suppurations and in the sputum. When recovery from typhoid fever is evident, *Salmonella typhosa* is usually eliminated from

the patient's body within a few weeks or months thereafter. Occasionally this does not happen. The patient seems to be unable to get rid of the bacilli, but under these conditions a specific bodily resistance develops in the affected one which holds the bacilli dormant in the tissues. However, if these apparently dormant bacilli retain their virulence and if the host is capable of harboring and growing virulent bacteria within the body without causing manifestations of the disease, that person is known as a carrier. In addition to those who continue to harbor and to discharge typhoid bacilli after recovering from the disease, there are a certain number of so-called healthy carriers who give no history of ever having had the fever.

Typhoid carriers have been designated as intestinal carriers, gallbladder carriers, hepatic and biliary duct carriers, depending on the situation of the focus capable of producing virulent organisms Occasionally there is a chronic urinary carrier, but these are less common than the chronic fecal carriers.

A diagnosis of the carrier state can be made only by a demonstration of the typhoid organisms in some of the secretions The carrier state cannot be diagnosed on the basis of serologic reactions The person who has active typhoid fever and the so-called healthy person who is a carrier are the most dangerous sources of the disease to the community

PROPHYLACTIC VACCINATION AGAINST TYPHOID AND PARATYPHOID FEVERS Travelers into regions where the water supply is unsafe or uncertain, those living in rural regions who have shallow wells for water supply, families of typhoid fever patients, physicians, nurses, and others in attendance are exposed to the infection and may contract it despite sanitary regulations and should be protected by vaccination or active immunization. *Salmonella paratyphi* and *Salmonella schottmuelleri* are included with *Salmonella typhosa* in the preparation of typhoid vaccines. Often commercial vaccine does not contain the paratyphoid organisms Typhoid vaccines are administered subcutaneously, intracutaneously, and by mouth The intracutaneous method is the best of the three methods, since it is sure of conferring immunity and is followed by less reaction than the other methods.

The reactions to the subcutaneous injection of typhoid fever vaccine occur within 24 hours to 48 hours There are local tenderness and swelling about the site of the injection In rare instances an abscess forms.

The general reactions, if any be present, consist of headache, malaise, fever, chills, and occasional nausea and vomiting, and in a few instances there is diarrhea The patient may be incapacitated for from 1 to 2 days. These reactions follow most frequently the second injection of the vaccine There is less likely to be a reaction after the injection if the patient does not exercise, and if he eats a restricted diet.

PATHOLOGY The demonstrable lesions begin by a preliminary hyperplasia of the reticuloendothelial system of the Peyer's patches of the intestines As the disease advances, there is sloughing, leaving shallow ulcerations parallel to the long axis of the intestines The ulcers heal as the disease regresses and leave no scars after healing.

The spleen is enlarged from reticuloendothelial hyperplasia Focal necrosis in the liver, in the meninges and in the periosteum is commonly observed The tibiae and the vertebrae are the bones most commonly affected by such a necrosis

If hemorrhage has occurred, it may be difficult to determine which ulcers were its source Perforation of the ileum with an ensuing peritonitis may be present.

More than one half of those who have typhoid fever are between 12 and 35 years of age. The sexes are equally affected. House infection occurring in one member, and usually in several members, of a family is common. Boys often are infected while swimming in the water of polluted streams. Sporadic instances of typhoid fever occur which are usually due to contact infection, often from carriers. The morbidity from typhoid fever is the highest in the summer and autumn months Incidence is least from January to April The incubation period is variable, usually from 8 to 1[illegible] days. However, the incubation period may be from 1 day to 3 weeks. [illegible]

SYMPT[illegible]

Anorexia, [illegible]

first thing, however, that makes the patient aware that all is not well is the presence of a fever. Typhoid fever is classically described as following a characteristic course. The fever gradually rises. This rise has been called the stadium incrementi (lasting about 1 week). The fever then reaches a level or establishes itself at about the same height (lasting about 1 week). This continuous fever is called the acme. After the acme the fever becomes markedly remittent (1 week to 10 days later). This remittent fever is called the amphibolous stage and finally ends by lysis. The lysis is called the defervescence. Immediately following the lysis there are a few days of subnormal temperature. The earlier clinicians classified the fever and the clinical symptoms of typhoid diseases according to the weeks of the disease. This practice is schematic and of very little value to practical diagnosis.

Accompanying the fever as the disease develops there are headache, pain in the back, chilly sensations, sometimes actual rigor or chills, anorexia, disinclination for exercise, nosebleed, slight abdominal distention, rarely diarrhea and usually constipation.

Examination after the fever has become fully developed reveals a slow pulse when contrasted with the elevation of the temperature. The pulse is often dicrotic. Sometimes coarse rales are heard in the lungs The spleen is often palpable. The psyche may be a little dull There is rarely delirium before the second week of the disease. The skin is dry and hot. It is infrequent for herpes or signs of coryza to appear early in the course of the disease

All the subjective symptoms are exaggerated until about the tenth day, when the patient no longer complains of the headache and becomes more apathetic and dull. This apathy and mental dullness is present during the course of many severe fevers, and it is designated as the typhoid state. Now the patient may become restless and delirious The delirium is more characteristically manifested during the night hours than in the daytime In the severer forms of the disease jumping of the tendons (subsultus tendinum) may be noticeable. If the typhoid state is well developed, there is a tendency of the patient to pick at the bedclothes (carphologia). Involuntary urination and defecation are common in delirious patients

Intestinal hemorrhage is common during the last part of the second week. The hemorrhage may be just a diapedesis of blood from the hyperemic, spongy, swollen Peyer's patches along the small intestine. As the danger of intestinal hemorrhage decreases at the beginning of the third week of the disease, the danger of perforation of an ulcer with subsequent peritonitis increases.

Variations in the severity of the symptoms of typhoid fever are great. In some instances the fever is never high and does not last more than a few days In others during the first few days or weeks the fever is high and then quickly disappears (typhus abortivus). The symptomatology in abortive typhoid resembles that of typhus fever or Brill's disease. In still other cases the patients continue to be up and about (walking typhoid).

During the fourth week of the disease recrudescence or relapse may occur. In these, the fever begins to subside over a period of several days Then there is a rise and the fever may remain up for several days to weeks. Recrudescence or relapse of typhoid fever may recur more than once, for as long as 2 months after the disease Recrudescent typhoid fever usually is of shorter duration and often is less severe than the first attack

Examination. The pulse rate is slow, out of proportion to the height of the fever. During the first 7 or 8 days a scattered petechia-like skin eruption, rose spots, may be observed intermittently on the abdomen, the thorax, and the back. When present, these spots are helpful diagnostically. The spleen as a rule becomes definitely palpable during the second week. Abdominal distention is present from the onset, but it is more marked as the disease progresses There may be a considerable amount of intestinal noises and gurgling on palpation.

Bedsores are likely to develop in the patients who are very ill. The points of pressure, the lumbosacral regions, are most likely to be involved by bedsores or decubitus ulcers

Bronchopneumonia with an ensuing circulatory failure may be present in those seriously ill In 3 or 4 weeks, if the patient survives, there is a fall of temperature by lysis, the *stadium decrementi*. The pulse rate, which has been increased after the slow pulse in the beginning, again decreases and there may be a definite bradycardia.

In patients who have been very ill, who have become greatly exhausted and emaciated, a posttyphoid psychosis may develop These posttyphoid psychoses are exhaustion psychoses and usually clear up when the patient has regained some of the lost body weight and strength

There is almost always leukopenia, the total leukocyte count not exceeding 7,000 or 8,000 per cubic millimeter of blood Often the leukocyte count is as low as 3,500 cells per cubic millimeter In many instances there is a relative increase in the large mononuclear cells The leukocyte count promptly increases, however, if a complication such as intestinal perforation occurs The blood culture is positive during the first week of the disease The Widal reaction is negative during the first week. If the Widal reaction is positive during the first week of the disease, caution is used in its interpretation, for the patient may have had typhoid vaccination.

DIAGNOSIS. *The diagnosis of typhoid fever is based on the demonstration of Salmonella typhosa* in the blood, feces or urine or on sternal aspiration There is no one symptom nor even a combination of clinical data which will suffice for making a definite diagnosis other than demonstration of the organisms of typhoid fever. A combination of fever, slow pulse, rose spots on the skin and palpable spleen usually indicates typhoid fever However, this combination of symptoms is rarely present in sporadic cases It is observed in districts where typhoid occurs epidemically and in a severe form.

COMPLICATIONS The complications of typhoid fever are (1) those which arise locally from the destructive effects of the intestinal lesions, (2) those referable to the septicemia, and (3) those which may arise as the result of prolonged fever and wasting of body tissue

The local complications arise from ulceration and necrosis of the Peyer's patches and are manifested by intestinal hemorrhage and intestinal perforation

Intestinal hemorrhages are more frequent during the second and third weeks of the disease than at other periods The bleeding may occur as a single hemorrhage or as a series of hemorrhages The bleeding may be insignificant in amount or large enough to be fatal. Large hemorrhages are the commonest cause of death in typhoid fever

Intestinal perforation and peritonitis are less common than hemorrhage The perforation usually occurs during the third, fourth, or fifth week of the disease but may occur as long as three months after the fever has subsided, and is likely to develop during or soon after straining defecation. The site of the perforation is usually the base of an ulcer situated toward the lower end of the ileum or even in the colon.

Surgical treatment is ineffective for hemorrhage in typhoid fever It may be curative in perforation and should be carried out immediately.

During the period of the septicemia, as in any septicemia, the complications which may arise are carditis or myocardial insufficiency, pneumonia, meningitis, osteomyelitis and furunculosis. Cystitis and at times nephritis may occur. Typhoid parotitis occurs in some cases

Complications arising from the presence of prolonged fever are mainly venous thrombosis in the deep veins of the pelvis or in the upper part of the leg An attack of typhoid fever often leaves a patient with a swollen edematous leg; the swelling and edema may clear up but often are permanent. In regions where typhoid fever

is rampant, there may occur a combination of venous thrombosis involving the leg from the hip downward and osteomyelitis involving the bones of the same leg. Typhoid osteomyelitis often settles in the tibia Frequently it is an exceedingly chronic disease. For years an open sinus which on occasions discharges small pieces of bone may persist (see p. 279)

Salmonellosis and Gastroenteritis. The usual sources of human salmonellosis are human carriers The organisms may be obtained in insufficiently cooked pork and fowl; eggs, water; food contaminated by rodents during storage; pets and farm animals.

About 160 strains or "types" of salmonella have been described. These strains differ from each other in their serologic and biochemical behavior.

The *Salmonella paratyphi* organisms cause (1) a disease which simulates typhoid fever, recognizable as different from true typhoid fever only by isolation and identification of the specific paratyphoid organism, and (2) a type of food poisoning in which after a short incubation period, a few hours, there are symptoms of gastroenteritis which are often explosive and severe.

A diagnosis can be established by isolation of the specific organism

Salmonellosis and Food Poisoning. Food poisoning by bacilli of the salmonella group occurs epidemically when rats and mice have access to human food and contaminate it with urine and feces. The common food vehicles for a spread of salmonellosis are cheese, milk, meat, sausage, salami, milk products, mayonnaise, chicken salad, and cured fish

There are two characteristics of salmonellal food poisoning: (1) all persons who partake of the food are affected, (2) salmonellal infection of the intestinal tract requires a long incubation period, sometimes 3 days, after ingestion of the food. When there is no infection of the intestinal tract, the symptoms of food poisoning in those who have a salmonellal infection begin from 6 hours to 3 days after ingestion of the food

The symptoms commence with severe cramps in the abdomen, and diarrhea, tenesmus, nausea and vomiting may occur In the more acute forms there may be fever and prostration In the acute stage of food poisoning by salmonella, it cannot be determined whether there is an infection or whether the poisoning is due to food intoxication The symptoms of the acute phases of salmonellosis are identical with those of shigellosis.

The diagnosis is made by the isolation of the organism by bacteriologic technics.

Salmonella septicemias are not clinically distinguishable. They follow food infection. During the course of the septicemia, foci of infections may occur and persist in the pelvis, gallbladder, kidney, heart, lungs, bones or any other tissue of the body. A chronic carrier state may persist, usually in the gallbladder. *Salmonella choleraesuis* is the common organism present in these infections.

THE FRIEDLANDER ORGANISMS

The organisms of the Friedlander group are short, nonmotile, nonspore-forming, gram-negative bacilli which characteristically possess large capsules They occur in the nose, mouth and intestinal tract of normal persons, in the lungs of patients with pneumonia and other respiratory diseases, and in suppurative infections of other parts of the body away from the respiratory tract They are enteric bacteria.

Klebsiella pneumoniae. *Klebsiella pneumoniae* is known also as Friedlander's

In recent years it has been learned that *Klebsiella pneumoniae* is important in the production of disease outside of the respiratory tract. The gastrointestinal and biliary tracts account for more than half of all the infections caused by this organism.

The biliary and urinary tracts when affected by stone, neoplasm or external pressu are easily rendered susceptible to infection by *Klebsiella pneumoniae*, and sep cemia, hepatic abscesses, meningitis, pelvic abscesses and subphrenic abscesses ma their appearance.

The symptoms are those of localized or generalized infection (septicemia often of a severe degree. Of late it has been recognized that *Klebsiella pneumoni* infections may also run a chronic course, and that they occur in many extrapu monary lesions.

The findings on examination depend on the situation of the lesions or lesio Isolation and identification of *Klebsiella pneumoniae* is the only means of diagnosi

Klebsiella pneumoniae may be isolated in blood from a patient who has a se ticemia, although the portal of entry may remain obscure.

THE VIBRIO COMMA AND ASIATIC CHOLERA

The causative organism of Asiatic cholera, type species Vibrio comma of the gen Vibrio, tribe Spirilleae and family Pseudomonadaceae, has long been termed the comm bacillus

It is generally agreed that vibrios carry an endotoxin and infect only man. The remain viable in feces and in river water for more than 2 weeks, and in sea water fo less than 1 week.

Immunity following recovery from cholera is of uncertain duration. It lasts fro 6 months to a year. The vaccine is prepared and administered in the same manner a typhoid vaccine It may be administered along with triple typhoid vaccine.

Cholera *has its endemic center in Asia Epidemics and pandemics are prevalen* along the rivers in the East and Middle East. In times past cholera epidemics oc curred along the Mississippi River and some of its tributaries. The *Vibrio comm* may be harbored in the biliary passages of human beings, and these persons ar carriers The presence of cholera means food contaminated by insects and rodents or drink containing the vibrios, or both.

The intestinal wall is irritated by the toxic action of the vibrios which remai localized in the intestinal tract Invasion of the blood stream is unknown. In th rapidly fatal infections there is insufficient time for extensive pathologic change to tak place *In more prolonged illnesses the mucosa of the small intestine is deeply injecte* and may show areas of sloughing Sometimes most of the small bowel is denuded of it epithelial lining The kidneys may reveal a toxic nephrosis

SYMPTOMS The symptoms of cholera commence with a profuse watery diarrhea and vomiting The diarrhea may be painless or associated with abdominal cramps Quickly the stools become colorless and thin and contain small white flocculi in suspension (rice-water stools). Enormous quantities of rice-water stools are dis charged during a 24-hour period The vomitus usually assumes the same rice-water appearance as the stools The abdominal cramps may be agonizing in character. As vomiting and diarrhea continue cramps appear in the muscles of the arms and legs The muscles become acutely contracted. Often the patient rapidly passes into a state of collapse and dies in from 10 to 12 hours after the onset.

EXAMINATION. Owing to the rapid loss of fluid by the diarrhea and vomiting, the cheeks are sunken in appearance, the nose becomes pinched and thin, the eyes are retracted and the eyeballs are soft, and the skin and the fingers are shriveled. The surface of the body is cold and wet. Respirations are rapid and shallow, and the patient may not be able to speak. Often a whisper asking for water is the only attempt made at speaking. The pulse is thready, weak and rapid. Rectal tempera- ture varies from 101 to 105 F (38 3 to 40.5 C). The patient is restless, throws his arms and legs aimlessly around until his strength fails As long as strength permits and consciousness is present he asks for water.

Recovery may be obtained by the rapid parenteral administration of fluids If the patient recovers, there is a gradual cessation of vomiting and purging, the pulse

at the wrist soon becomes palpable, and there is a return of some of the warmth to the surface. On continued administration of fluids, the secretion of urine returns and the recovery may be remarkably fast.

DIAGNOSIS The diagnosis is established by isolating the cholera vibrio from the stools and sometimes also from the vomitus of patients. By the time the diagnosis is thus attained, the patient from whom the material for culture was obtained is dead or is well on the road to recovery. However, these procedures must be carried out to make sure that the disease is cholera and if so to set up controls for protection of those still well.

In the presence of an epidemic the disease may be clinically recognized by the suddenness of the onset, the severity of the symptoms and the rapidity of the course which distinguishes it from all other diarrheal diseases. Sporadic and mild infections with *Vibrio comma* are more difficult to recognize.

Epidemiology Unit No 50 in 1945 reported a study of cholera in Calcutta. Some 400 patients were divided into 5 groups, group A being treated with sulfaguanidine, group B kept as a control, group C treated with sulfadiazine, group D treated with penicillin and group E treated with sulfadiazine and penicillin combined. Seemingly the most beneficial therapeutic agent was transfusions of blood plasma and not chemotherapy Of 35 severely ill patients treated with plasma plus chemotherapy, none died Of 19 similar patients treated with chemotherapy alone; 3 died, and of 24 control patients 23 died Rehydration will effectively lower the expected death rate in cholera. The addition of adequate amounts of blood plasma to the therapy of cholera will further improve the chance of recovery.

THE BRUCELLAE AND BRUCELLOSIS (USUALLY MILK BORNE)

(*Malta Fever, Melitococcosis, Mediterranean Fever, Rock Fever, Gibraltar Fever, Texas Fever, Rio Grande Fever, Neapolitan Disease, Bang's Disease, Brucellosis*)

The genus *Brucella* is of the tribe Brucelleae of the family Parvobacteriaceae. Three species are found in manifest and in latent infections. *Brucella melitensis* (*Bacterium melitense* Bruce, *Micrococcus melitensis*, *Alcaligenes melitensis*, caprine Brucella), *Brucella abortus* (*Brucella melitensis* var *abortus*, *Alcaligenes abortus*, abortion or Bang's bacillus, bovine Brucella) and *Brucella suis* (*Brucella melitensis* var. *suis*, porcine abortus strain)

These organisms are cosmopolitan in distribution The organisms of bovine origin more easily affect man Caprine infections are obtained from the milk of goats and cheese made from this source

The production of artificial immunity in animals by means of vaccines consisting of living brucella of reduced virulence has been accomplished. In common use for vaccines are the strains S19 and 45 of *Brucella abortus*. The avirulence of the strains used for vaccination is only relative and occasionally may cause the disease when used for purposes of vaccination. Undulant fever in human beings has been caused by vaccination.

The agents of infection enter the body through the mouth or through the skin. The organisms entering through the mouth may gain entrance to the tissues by passage through the lymphatic system in the throat or the mesenteric lymph nodes. Once inside, the infection is spread through the blood stream The nodular reactions are evidences of the response of the reticuloendothelial system to the presence of the bacterial proliferation. The renal pathologic changes may be due to the elimination of brucella through the glomeruli.

Brucellar lesions are infectious granulomas They appear in varying sizes as the result of repeated disseminations of the organisms into the blood stream. The occasional suppurative lesions in various organs illustrate the ability of these organisms to grow in different tissues.

The disease is acquired by drinking contaminated milk or by contact with an infected animal.

SYMPTOMS. The average incubation period in man varies from 5 to 30 days. The infection may be manifested as a subacute septicemia or as focal or localized infections. When granulomas form, the disease is chronic.

The symptoms commence with excessive fatigability, weakness, headache and backache The temperature rises slowly to 102 to 105 F (38.9 to 40.5 C). There are chills and profuse sweating The average duration of the febrile period in a severe infection is about 3 months. However, the fever usually lasts from 3 to 5 days to 10 to 20 days. Often there is one long febrile period which subsides by lysis. However, repeated relapses of fever may occur within 2 years after the initial infection Relapses of fever may remind the physician of the possibility that brucella organisms may be causing the patient's illness

A loss of appetite and constipation are incident to the fever. The patient, despite daily fever, may appear comfortable and well. A mild obstructive jaundice may develop. This stage of the disease may progress to a more chronic form, or a chronic brucellosis may be the primary manifestation of the infection.

In chronic brucellosis the symptoms are vague and not particularly characteristic of any infectious diseases. They are fatigability, myalgias, arthralgias, neuralgias, headache, giddiness, ocular fatigue, sweating, nasal catarrh, chronic sore throat, often cough, tachycardia, irritability, depression, and various disturbances of digestion Women often have menstrual and reproductive disturbances

A definite type of chronic spondylitis is caused by an infection with brucella (see Diseases of the Bones, Chapter 7) In almost one half of these patients transient arthritis may be present. The arthritis comes on suddenly and is severely manifested in the hip, knees, shoulder and ankle joints. It usually clears in from 3 to 5 days or persists

During the chronic stage lesions of the central nervous system may reveal themselves These symptoms are those of a subacute or chronic meningitis associated with a pleocytosis of 150 to 200 cells in the spinal fluid with the lymphocyte prominent in the count As the meningitis subsides signs of meningomyelitis and focal cerebral lesions manifested as monoplegia, paraplegia or hemiplegia may appear. Organisms can be cultured from the spinal fluid The protein concentration of the spinal fluid is increased

An endocarditis may become manifested which cannot be suspected from symptoms alone Bronchopneumonia is a serious manifestation of this disease.

EXAMINATION. The physical examination is destitute of findings which may indicate the seriousness of the disease. The physical findings if any will depend on the localization of the infection. In the chronic forms there may or may not be a low-grade fever at the time of the examination. The liver may be slightly enlarged. The heart may be enlarged and there may be systolic murmurs There may be an increased redness of the mucous membranes Often there is more than the usual sensitiveness on palpation of the lower part of the abdomen on the right side. The joints may be swollen and tender Leukopenia usually is present during the acute stages of the disease. However, moderate leukocytosis occasionally occurs There may be lymphocytosis during all phases of the disease An increase in the numbers of lymphocytes is accompanied by immaturity. The erythrocytes in the chronic stages of the disease may be somewhat reduced in number and there may be a mild macrocytic hypochromic anemia

DIAGNOSIS. The diagnosis of brucellosis is definitely established by isolation of the organisms from the lesion, blood, urine, or feces Isolation of the organisms bears no definite relation to any given stage of the disease nor to the presence of organisms in the blood. Positive blood cultures have been obtained as early as the first day of illness and as late as a year or more subsequently. The organisms are excreted irregularly in the urine and in the stools. They can be recovered from

the spinal fluid and pus in instances of meningeal involvement or in suppurative lesions.

Agglutination tests are diagnostically helpful In instances of suspected brucellosis a negative response to agglutination tests may be helpful in eliminating the possibility of the disease

Agglutinin titers of 1:80 or more occur in about 90 per cent of brucellar infections by the end of the second week and may eventually reach 1:10,240. Agglutination titers of more than 1:200 in the presence of clinical symptoms suggestive of brucellosis constitute presumptive evidence of active infection. In the absence of symptoms an agglutination titer of 1:80 may be evidence of frequent exposure but it is not diagnostic.

Many other diagnostic tests have been employed, for instance, the bactericidal test and the opsonocytophagic test These tests are valuable in the hands of trained observers accustomed to making the proper interpretations of the response provoked by the test.

THE PASTEURELLAE (FLEA BORNE—AIR BORNE)

Pasteurella pestis and the Plague. *Pasteurella pestis* of the genus *Pasteurella*, tribe Pasteurelleae, family Parvobacteriaceae, is the cause of plague.

Pasteurella pestis has two antigens. Cultures with well-developed antigens agglutinate in specific immune serum. Antigens are heat-labile. The vaccine now used is an alcohol-precipitated vaccine.

Plague is primarily a disease of wild rats and other rodents and is transmitted from one to another by the bites of infected fleas (see Fleas, Chapter 20). Infections in man are accidental, from the bite of infected fleas, except in the pneumonic type in which the organisms are inhaled

Plague is endemic in various parts of the United States, and occasionally human infection occurs

In the western states human infection formerly had been observed only in California, but in recent years infections have been observed in Oregon, Montana, Idaho, Nevada, Utah, Wyoming, Washington, Arizona, New Mexico, Colorado, North Dakota, Oklahoma, Kansas, and Texas Surveys have been conducted in more than 600 counties of the 17 westernmost states, and plague has been found nearly 4,000 times in the wild rodents of 132 counties of 15 of these states.

An attack of plague often confers a lasting immunity. The immunity following a natural plague infection is probably relative, for recovery from the natural disease has in a number of instances been followed by a second infection

In India vaccination reduces the risk of contracting plague to one fourth and the risk of death to one eighth. In Java the death rate was reduced to an average of 17.5 per cent. It fell from one fourth to less than one twenty-fifth of the original mortality in the course of a 5-year vaccination campaign

Pasteurella pestis produces in man three types of disease which are termed respectively bubonic plague, pneumonic plague, and septicemic plague. The origins of bubonic plague and pneumonic plague are related to the portal of entry of the pasteurella When the infected fleas bite the lower extremities, the plague bacilli spread rapidly through the lymphatic structures and there is an enlargement of the lymph nodes in the groin These enlarged lymph nodes are termed *buboes;* hence *bubonic plague* The lymph nodes rapidly become necrotic and suppurate, and abscess formation and septicemia ensue. Foci may be established in the lungs and elsewhere in the body

When infected droplets of moisture containing the bacilli are inhaled, the speedily ensuing infection is termed *pneumonic plague* There is a severe, widely dispersed pneumonia which involves the lungs completely Severe respiratory failure with deep

SYMPTOMS The average incubation period in man varies from 5 to 30 days. The infection may be manifested as a subacute *septicemia or as focal or localized* infections When granulomas form, the disease is chronic.

The symptoms commence with excessive fatigability, weakness, headache and backache The temperature rises slowly to 102 to 105 F (38 9 to 40.5 C). There are chills and profuse sweating The average duration of the febrile period in a severe infection is about 3 months. However, the fever usually lasts from 3 to 5 days to 10 to 20 days. Often there is one long febrile period which subsides by lysis. However, repeated relapses of fever may occur within 2 years after the initial infection. Relapses of fever may remind the physician of the possibility that brucella organisms may be causing the patient's illness

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patient from whom the material for culture was obtained will be dead. Bacteriologic study, however, is necessary, for by the time the laboratory renders the report, other patients will have come under observation who contracted the disease from the original patient. The diagnosis in this instance is then certain.

DIAGNOSIS. The diagnosis depends on obtaining and identifying the *Pasteurella pestis*. The sputum does not show the *Pasteurella pestis* in the early stages of the disease. Blood cultures are of no great help in establishing an early diagnosis. Bacteremia usually does not occur until the last day or two of the illness. In an epidemic early and frequently repeated bacteriologic examinations of the sputum by an experienced examiner are necessary in order to make the correct diagnosis

The primary pneumonic form of plague is most difficult to differentiate from infection by the streptococci or pneumococci or from an influenzal type of bronchial pneumonia.

It is impossible to differentiate pestis minor from tularemia except by agglutination tests and blood cultures

Pasteurella multocida and Hemorrhagic Septicemia (Bites or Contacts). *Pasteurella multocida*, which causes hemorrhagic septicemia in animals, is indistinguishable from *Pasteurella aviseptica, Pasteurella bollingeri, Pasteurella suiseptica, Pasteurella muriseptica*, and *Pasteurella cuniculicida* All are coccobacilli and gram-negative They are all closely related, are saprophytic and parasitic and are capable of infecting many different animals Individual susceptibility in all species of animals and in man varies from extreme susceptibility to complete resistance.

Human infections with *Pasteurella multocida* may not be suspected. In suspected instances of the infection the disease follows animal bites or exposure to carcasses of cattle, pigs, or rabbits. The consumption of infected rabbits may cause enteritis, conjunctivitis, and appendicular abscesses In the septicemic distribution of the infection the symptoms vary widely and may be manifested by recurrent chills and fever, pneumonia, empyema, meningitis, and puerperal sepsis

The diagnosis is established by identification of the organism bacteriologically.

Pasteurella pseudotuberculosis. The large, gram-negative, elongated *Pasteurella pseudotuberculosis* organisms are pleomorphic.

Pasteurella pseudotuberculosis causes spontaneous infections in rodents, pigeons, turkeys and canaries In a small number of human infections it has been isolated from the blood stream during life, and from the characteristic necrotic lesions at necropsy. The mode of infection is not known.

There is a prodromal feeling of being unwell followed by an acute onset with headache, chills, fever, and general pains in the extremities and back. The fever is of an irregular or remitting type as observed in septicemia At times the temperature reaches 105 F (40 5 [illegible] e
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serous cavities as a further indication of the septicemia.

The diagnosis is accomplished by identification of the organism through bacteriologic procedures

Pasteurella tularensis and Tularemia (Contact, Insect Bites). The species [illegible] remia, belongs [illegible] The organism [illegible] rugged surviving power It has been known to have survived for weeks in hides, and for months in carcasses and in water

Pasteurella tularensis causes a specific infectious disease of wild mammals in which it is maintained as a heterogeneous infection through a variety of insects acting as reservoirs and vectors

Tularemia is known to occur in the ground squirrel, hare, rabbit, guinea pig, woodchuck, muskrat, wild rat, wild mouse, European water rat, opossum, kitten, young coyote, grouse, quail, sheep and gray fox. The red fox is not infected. When the infec-

cyanosis and death ensue. The deep cyanosis and rapidly fatal course originated the term Black Death in the fourteenth century The pneumonic form of the disease is likely to predominate during the early period of an epidemic.

It is to be remembered that the patient who has pneumonic plague is likely to infect doctors and other attendants of the sick one and that even adults attending funerals of those dead from plague may become infected.

When the portal of entry is not definite, during the course of one of the conventional forms of plague, septicemia may be the dominant manifestation and thus the disease deserves the name *septicemic plague*.

Another form of the disease, *sylvatic plague*, is transmitted by the bite of a flea which normally feeds on wild rodents This disease in man differs somewhat in details from the ordinary forementioned types of plague. The fleas bite on the upper extremities, and the original buboes occur in the axillae. This form of plague frequently changes to pneumonic plague In this variety of plague the role of fleas in the transmission of *Pasteurella pestis* is established experimentally.

In the rural regions of sylvatic plague men and children who handle or play with wild rodents are more frequently attacked than are others who do not indulge in such practices.

SYMPTOMS. After an incubation period of 2 to 6 days the symptoms commence with a chill. The temperature increases to 101 F (38 3 C) and may be as high as 105 F (40 5 C) The fever is associated with severe generalized headache; often there is vertigo, and soon extreme prostration ensues In bubonic plague the early symptoms are those of a severe infection. In pneumonic plague the inception of the disease and the onset of symptoms often resemble those of an acute influenza of the respiratory type There are fever and chills and dry cough, associated with increased respiratory and pulse rates. The cough soon is productive of frothy, blood-streaked sputum which later becomes grossly bloody

In all forms of plague the intoxication is extreme. There are a rapid pulse, a bluish or definitely cyanotic color of the face, delirium, and a rapid decline Death occurs within a week from the onset of symptoms. In debilitated victims plague is characterized by extreme intoxication, increasing from hour to hour, and death occurs before any physical signs of the disease can be detected.

Pestis Minor In contrast to the serious types of plague, there is a form of the disease which often is called pestis minor In pestis minor the patient may be up and about and able to carry on his usual occupation, unaware of fever or of swollen lymph nodes Pestis minor is not so contagious as the other types of plague.

EXAMINATION After the general signs of infection have been present for 24 or at most for 48 hours, the bubo usually is found on examination. It is the enlargement of a solitary lymph node, at first no more than 1 cm. in diameter, moderately firm and tender to pressure As the disease develops, more nodes may become involved and may become adherent to each other. The periglandular tissue and overlying skin are edematous and inflamed The bubo may be situated in any part of the body, but it usually is in the inguinal region In 1 case out of 5 it is situated under the arms and in only 1 case in every 10 is the bubo in the cervical region. In 1 to 3 days after the onset of fever with or without the known presence of the bubo, minute hemorrhagic spots may appear in the skin.

[illegible] informative There [illegible] lobe of the [illegible] ionia, is not present Plague pneumonia is of a lobular type which may later coalesce to involve the whole lung if the patient lives long enough. Leukocytosis is present.

Puncture of a much swollen lymph node with a fine needle and aspiration of a few drops of its contents for bacteriologic examination may be done. By the time the bacteriologic examination is finished, there are 6 chances out of 10 that the

patient from whom the material for culture was obtained will be dead. Bacteriologic study, however, is necessary, for by the time the laboratory renders the report, other patients will have come under observation who contracted the disease from the original patient.

DIAGNOSIS. *Pasteurella pestis* The sput tages of the disease Blood cultures are of no great help in establishing an early diagnosis. Bacteremia usually does not occur until the last day or two of the illness In an epidemic early and frequently repeated bacteriologic examinations of the sputum by an experienced examiner are necessary in order to make the correct diagnosis.

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There is a prodromal feeling of being unwell followed by an acute onset with headache, chills, fever, and general pains in the extremities and back The fever is of an irregular or remitting type as observed in septicemia. At times the temperature reaches 105 F (40 5 C) Anorexia, abdominal tenderness, constipation and variable degrees of leukocytosis are usual Within a few days after onset the liver, and sometimes the spleen as well, become palpable and tender There may be effusions into serous cavities as a further indication of the septicemia.

The diagnosis is accomplished by identification of the organism through bacteriologic procedures

Pasteurella tularensis and Tularemia (Contact, Insect Bites) The species *Pasteurella tularensis* (*Bacterium tularense*), which causes the disease tularemia, belongs to the genus *Pasteurella,* tribe Pasteurelleae and family Parvobacteriaceae. The organism is pleomorphic Both ovoid and bacillary forms exist. This organism has a rugged surviving power. It has been known to have survived for weeks in hides, and for months in carcasses and in water.

Pasteurella tularensis causes a specific infectious disease of wild mammals in which it is maintained as a heterogeneous infection through a variety of insects acting as reservoirs and vectors

Tularemia is known to occur in the ground squirrel, hare, rabbit, guinea pig, woodchuck, muskrat, wild rat, wild mouse, European water rat, opossum, kitten, young coyote, grouse, quail, sheep and gray fox. The red fox is not infected. When the infec-

tion occurs in summer, it is usually acquired by the bite of an insect, for instance, the deer fly or horse fly

The insects known to carry tularemia are the deer fly, ticks and stable flies. When the infection occurs as the result of transmission by the wood tick, it is not necessary that the tick ever should have had direct contact with an infected animal, for it has been shown that there is hereditary transmission of the infection by female wood ticks to their eggs, larvae and nymphs Ticks harbor the infection throughout the winter and thus keep it active from year to year. The tick, therefore, constitutes the principal means for the natural transmission of the disease. The arthropods directly related to human diseases are the Rocky Mountain tick (*Dermacentor andersoni*), the Western wood tick, the common Eastern dog tick, the Lone Star tick and the deer fly (*Chrysops discalis*) The mosquito (*Aedes cinereus*) in Sweden may transmit tularemia

Infection as a result of eating of infected flesh is rare because the germ is destroyed readily by cooking of the meat Tularemia could appear in epidemic form if a number of persons partook of insufficiently cooked infected flesh. The infection most commonly is acquired by the dressing and handling of the infected animal or bird or the wearing of infected clothing, such as gloves, or the use of infected hand towels.

The infection is most prevalent in the summer, when it is transmitted by ticks and by flies. The incidence of the disease is increased during the hunting season on cottontail rabbits, usually from November to January.

An early but transitory bacteremia originates diffusely scattered foci of necrosis in the spleen, liver, lungs, lymph nodes and bone marrow The infection may involve the lungs, pericardium, pleura and peritoneum Tularemia produces a lobular type of pneumonia that is secondary to the general bacteremia There are hemorrhagic effusion, abscesses, and localized or general pneumothorax. With the appearance of antibodies bacteremia disappears, but new lesions may develop by lymphatic extension When the formation of antibodies is slow or insufficient to prevent it, the organisms are dispersed through both the systemic and pulmonary circulatory systems, resulting in the formation of miliary foci of necrosis in nearly every organ, and death ensues

SYMPTOMS In the usual instance of the disease, 3 or 4 days after contact, there develops a papule at the site of inoculation, often on the hand. In 7 or 8 days the papule becomes an open ulcer Synchronously with ulceration a regional lymphadenopathy appears. There is fever which lasts about 1 month. The fever, attended by chills, usually shows an initial rise, a remission and a secondary rise. There are anorexia, sweats, malaise, and headaches The acute stage is followed by a period of weakness and prostration lasting from 3 to 6 months. In about one third of those who have the disease the swollen lymph nodes may suppurate and discharge through the skin. The rest of the lymph nodes remain hard and discrete. In some instances suppuration may occur many months after clinical recovery has taken place.

In some the disease is manifested as a septicemia from its onset, or develops into a severe septicemia resulting in early death from the fourth to the eleventh or twelfth day

In a general way the symptoms depend on the portal of entry of the infection If the infection has been obtained from the inhalation of droplets of infected material, a pneumonic form of the disease develops. However, a pneumonia may arise in an ulceroglandular infection The onset may be sudden with a chill, fever, dyspnea, cough, pain in the chest and profuse sweating These patients appear extremely ill and frequently are suspected of having typhoid fever.

If some infected material is spattered into an eye, the primary lesions occur there. The primary ocular lesion is often situated on the lower lid.

Irrespective of how the disease gets to the eye, the infection is followed by general infection of the conjunctiva and lacrimal sac which is characterized by congestion, lacrimation, injury to the eye and involvement of the lymphatic structures.

Ingestion of *Pasteurella tularensis* causes a necrotizing pharyngitis, abscesses in

the roof of the mouth, enlargement of the submaxillary and cervical lymph nodes, and ulcers, hemorrhages and points of necrosis in the gastrointestinal tract.

EXAMINATION. The portal of entry or site of inoculation in the skin is revealed by the presence of an ulcer. From the site of inoculation the bacteria spread along the superficial and deep lymphatic structures, with the result that dermal lymphadenitis occurs and regional lymph nodes are enlarged in 9 of 10 cases. In the absence of discoverable primary lesions lymphatic invasion is not evident. The initial lesion and the lymph nodes are tender and painful Occasionally a maculopapular eruption is present on the arms, neck and chest In many cases the original lesion is *all that is ever present Secondary manifestations do not occur.*

The rest of the observations on examination depend on the complications, if any, which are present In the eye the infection causes the conjunctiva to become acutely inflamed, greatly swollen and very painful Multiple small, discrete, yellow nodules make their appearance on the conjunctiva and at the same time the periauricular, cervical and submaxillary lymph nodes become swollen and tender. The active inflammation lasts from 3 to 5 weeks and only rarely results in permanent scarring of the cornea or involvement of the media

The physical signs of tularemic pneumonia are those of a bilateral atypical pneumonia Physical examination of the chest may reveal no abnormal findings even though pleuropulmonary involvement can be demonstrated roentgenographically. In some instances the pneumonic consolidations resemble those in tuberculosis.

If the organisms reach the central nervous system, a severe meningitis ensues.

During the acute stage of tularemia either leukopenia or leukocytosis may be observed. Agglutinins do not make their appearance in the blood until after the second or third week of the disease Ordinarily the organisms cannot be obtained from the blood before the third day, nor after the twelfth However, in some instances the presence of agglutinins in the blood has been revealed 25 years after the patients have recovered from the disease

DIAGNOSIS The diagnosis preferably is established by isolation of the organism. There is usually an initial bacteremia for a week In some, the disease takes the form of a septicemia from the onset, and in these the cultures from the blood may be positive.

Pasteurella tularensis may be recovered during the first week of disease by inoculation of guinea pigs or by direct culturing into suitable mediums. Pus taken from suppurating lymph nodes early in the disease contains viable bacteria, but the late adenopathies usually prove to be sterile on culture. At necropsy the acute necrotic lesions in the liver, spleen, lungs and bone marrow readily yield viable organisms.

Specific antibodies appear in the blood during the second week, increase in the third week, and reach maximal titers in the fourth and fifth weeks. Tularemia serum agglutinates *Pasteurella tularensis* to a much higher degree than *Brucella abortus* or *Brucella melitensis*

Intradermal injection of antitularensis serum causes an immediate erythematous, edematous reaction which is bacterial specific. This test may be diagnostically useful, but it has not been generally used as such an aid

THE ANTHRAX BACILLUS (CONTACT)

Anthrax is primarily a disease of sheep, cattle, horses and swine. The spores of the bacillus remain viable in soil almost indefinitely In the United States, southeastern South Dakota, northeastern Nebraska, extending southward to include part of the Texas Gulf Coast and the lower Mississippi valley from Arkansas to and including the Delta region are particularly affected

tion occurs in summer, it is usually acquired by the bite of an insect, for instance, the deer fly or horse fly.

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[illegible] the lymphatic structures

[illegible] izing pharyngitis, abscesses in

perfringens, rarely sporulate. The natural habitats of the clostridia are the soil and the intestinal tract of higher animals and man.

Gas Gangrene Group. The five most important species of the gas gangrene group are *Clostridium perfringens*, *Clostridium novyi*, *Clostridium septicum*, *Clostridium bifermentans* and *Clostridium histolyticum*. All of these produce soluble toxins which can be neutralized by their respective antitoxins.

The clostridia of gas-forming gangrene have in common the ability to produce a rapidly spreading edema of the subcutaneous connective tissue attended by the formation of gas bubbles Blood vessels thrombose. Destruction of muscles ensues. The gas increases in the tissues, the skin acquires a dusty hue, and a tympanic note on percussion is present. A localized gas gangrene may be manifested by only a foul-smelling discharge containing gas bubbles

When the clinical evidence of the presence of gas gangrene is clear, the practice is to give a polyvalent antitoxin.

The *Clostridium tetani* infection has been considered in Chapter 6.

Clostridium botulinum (*Food Poisoning and Botulism*). Two subspecies of *Clostridium botulinum* have been identified and these different strains or subspecies or types produce specific toxins. The soil is the reservoir of these organisms. Their spores may be present on a wide variety of vegetables and fruits These organisms do not grow in the human body The disease termed botulism is a toxemia and not an infection. It follows the ingestion of preserved foods in which the organisms have grown and produced the toxin The preserved or inadequately cooked home-canned vegetables have been allowed to stand, and have been eaten without further cooking In Europe botulism results from eating smoked, salted or spiced meats In the United States the poisoning results from eating inadequately sterilized canned vegetables or fruits

SYMPTOMS. Usually several members of a family or a party who have consumed the same food are affected at the same time

From about 12 to 48 hours, or occasionally several days, after ingestion of the infected food there are nausea, dryness of the mouth with thick scanty saliva, vomiting, diarrhea, and dimness of near vision due to paralysis of accommodation The pupils are dilated and fixed but sometimes they may react even in fatal botulism Diplopia and ptosis of the eyelids are soon followed by abolishment of all ocular movements Articulation becomes indistinct and swallowing is difficult Food and drink are regurgitated through the nose or aspirated into the larynx

EXAMINATION. A general muscular weakness is present. The arms and legs cannot be voluntarily moved nor can the head be raised The muscles of respiration are weak and breathing is difficult One movement of a part may be performed but not repeated owing to fatigue The tendon reflexes are within normal limits of response. There is profuse sweating The pulse is rapid and feeble.

The mental condition is unaltered but when botulism is fatal, there may be terminal coma, stupor or convulsions In uncomplicated botulism the temperature is normal The spinal fluid shows no change Usually death occurs in from 4 to 8 days as a result of paralysis of respiration, circulatory failure, or pneumonia. If convalescence is possible, if the patient survives longer than a week, complete recovery is expected In instances of small doses of the toxin recovery is more quickly accomplished than when the dose [illegible]

[illegible] 12 and 48 hours or longer after eating poisoned foods, with the subsequent occurrence of bulbar palsy and finally general weakness of both smooth and striated muscles, are suggestive of botulism. The coincidence of a similar illness of several persons who partook of some of the same foods renders the diagnosis of botulism certain. The demonstration of the toxins or of the bacilli in aliquots of the food may be helpful in the diagnosis

The death rate averages 50 per cent In cases of survival, partial paralysis may persist for 6 to 8 months. In treatment for botulism polyvalent A and B antitoxin is used.

The disease in man is primarily a cutaneous infection which frequently progresses to a fatal septicemia. It affects dwellers in agricultural areas, but more usually workers in establishments where animal products, such as hides and hairs, are processed. The use of items such as shaving brushes or furs made from contaminated animal products may result in an occasional infection.

The pathogenesis of the disease is not fully explained. There is often evidence of a local lymphatic spread of the bacteria once the infection starts. Ultimately there may be bacteremia. The accumulation of bacteria in the blood stream may not be evident until shortly before death.

The incubation period is from 1 to 3 days.

The disease is suspected if a patient who has handled raw animal products such as hides or wool, or dead animals at a rendering plant, presents himself with a cutaneous lesion which has begun as a small red macule which enlarged and was followed, after 2 or 3 days, by local edema

The anthrax vesicle, filled with clear fluid, occupies a central position on the macule and soon spreads by vesiculation in a satellite fashion The lesion becomes necrotic, and the black eschar present in the older lesions is characteristic. The cutaneous lesion is not painful, but enlargement and tenderness of regional lymph nodes occur Malaise, fever and general prostration develop in accordance with the severity and extent of the infection.

Woolsorters' disease occurs in those who have handled wool of animals with anthrax The patient has a chill, fever, headache and pains in the back and legs. The respirations are rapid and attended by severe pain in the chest. There is cough but little expectoration. Examination reveals diffuse medium rales in the chest The temperature rises to 103 to 104 F (39 4 to 40 C) The heart sounds are enfeebled, and collapse and death occur in from 1 to 3 days

The fever rises rapidly and subsequently subsides.

In those in whom no primary lesion is present there may be great swelling of the eyelids, head, arms and hands. The edema may be generalized Areas of cutaneous gangrene may appear

Direct microscopic examination of material from a cutaneous vesicle or from an internal source may reveal the gram-positive rods and permit a tentative diagnosis. Detection of the organism is best done by inoculating mice with material from the lesion, blood, tissues, foods or articles suspected of being contaminated.

Anthrax often is a fatal infection Death may come in from 3 to 5 days. Those who recover do not have severe and rapidly progressive skin lesions

A feature of anthrax infection is the extreme fear and anxiety its presence engenders in the patient.

Anthrax Food Poisoning. Anthrax may be acquired from drinking the milk or eating the flesh of an infected animal The symptoms are those of intense bacterial food poisoning. There are vomiting, diarrhea, fever and pains in the abdomen, back and legs. Blood may be vomited or passed in the feces Soon cyanosis, anxiety, and feeble pulse and heart sounds are present to be followed by collapse and death in from 2 to 7 days The fever is not more than 100 F (37 8 C).

In some severe infections, endocarditis, peritonitis and meningitis are dominant manifestations.

The diagnosis is established by obtaining the anthrax organisms from the infected food or obtaining it from those infected by the foods

THE CLOSTRIDIA (PUNCTURE WOUNDS)

Organisms of the genus *Clostridium*, of the family Bacillaceae, order Eubacteriales, are anaerobic or micro-aerophilic rods, producing endospores. A few species, like *Clostridium perfringens*, produce capsules, the majority do not Some, like *Clostridium*

released by rupture of the bacterium and its conversion into a mass of bacteriophage or viral particles.

Some viruses, as revealed by biochemical studies, have a tendency to assume the crystallization forms. This may indicate that these particular viruses lie at the lowest level of life or on the borderline between life and nonlife Observations that some viruses resemble enzymes which can be synthesized in the laboratory seem, in a small way, to support this view

Luria learned that in the bacterial viruses considered to be composed of a number of vital elements several elements could be destroyed by ultraviolet radiation Evidence was advanced that a virus thus treated was singly unable to reproduce itself; when two or more partially destroyed viruses entered a single bacterium, however, an apparent combination of the remaining uninjured elements occurred, resulting in a new individual, which was able to reproduce itself and to destroy the bacterium.

Delbruck and Bailey studied the reproductivity and method of establishment of mutant strains of virus. Their work suggests an interchange of material between the parent viruses typical of the interchange of parent factors in formation of new individuals which is characteristic of sexual reproduction.

The implications are that viruses have a natural method for production of infinite numbers of new strains closely approximating the sexual mechanisms of higher organisms. The probabilities are that new disease-producing forms will occur frequently. However, new mutant strains of viruses may be produced for the benefit of all of us. For example, the 17D strain of yellow fever virus and vaccinia virus are mutations of the viruses of yellow fever and smallpox which are beneficial.

Viruses differ in their individual nutritional requirement or tropism. This variation may depend on only slight tissue or environmental differences The variation may reach to new cells or tissues, sometimes with complete loss of the initial tropism. It may occur independently of variation in the antigenic constitution of a virus.

Some authorities have adduced evidence from observations on bacteriophagy that the antigenic constitution of the host cell and susceptibility to a given virus are related The antigenic constitution may be associated with variation of tropism or may occur independently of it Variation of antigenic constitution has an important bearing on the serologic identification of viruses Such variations do not occur often, so that it has been possible to base much of what is known about differences among viruses on serologic observations

Viruses differ in their individual proliferative powers There are low-titer and high-titer viruses. Little is known regarding the factors which determine these individual differences They appear to be represented in both the host and the parasite Low-titer strains may not lack in invasiveness and may become widely disseminated in the tissues of the hosts Such strains may be partly responsible for subclinical infections and naturally acquired active immunity to individual viral diseases, for instance, poliomyelitis

It is not known how viruses act to produce injurious effects on the cells they invade. The lesions caused by viruses range from rapid cell death to stimulation of cell growth and multiplication The stimulation of cell growth is magnificently demonstrated by those viruses capable of the production of tumors.

Cell inclusion bodies may be produced by viruses and if so they are termed specific incl ... ises are termed nonspecific ... The formation of inclusion ... in cells which succumb quickly to a virus. The presence of characteristic inclusion bodies is diagnostically helpful, but their absence does not exclude the presence of a viral infection

The diseases caused by viruses are as varied as any other group of infectious diseases. Some viral infections occur regularly in a clinically evident form; others

LISTERIA MONOCYTOGENES AND LISTERELLOSIS

The *Listeria*, a genus of the family Corynebacteriaceae, are cosmopolitan in distribution. Species *Listeria monocytogenes* is the causative organism of listerellosis.

In children and young adults there are a septicemia, a purulent meningoencephalitis and local hepatic necrosis. The symptoms resemble those of other septicemias, purulent meningitides or encephalitis. There is a mononucleosis. The blood response may closely resemble that of infectious mononucleosis. However there is no known relationship between listerellosis and infectious mononucleosis

The spinal fluid contains *Listeria monocytogenes* and both mononuclear and polymorphonuclear leukocytes The blood contains a heterophil antibody which agglutinates erythrocytes of the sheep (a positive Paul-Bunnell test)

The diagnosis depends on the demonstration of the organism in the lesions of internal organs or from the spinal fluid.

ERYSIPELOTHRIX AND ERYSIPELOID (SKIN ABRASIONS)

Erysipelothrix rhusiopathiae differs from *Listeria monocytogenes* in being nonmotile and in manifesting a predilection for the skin, endocardium and joints. The disease erysipeloid is a localized cutaneous infection, although septicemia with endocarditis and involvement of joints may occur The infection confers no immunity

The infection develops subsequent to an abrasion incurred while handling fish or shellfish, meat or poultry. After an incubation period of from 2 to 7 days pain is present at the site of inoculation and is attended by edema and a brilliant purplish red erythema There is peripheral extension of the erythema with clearing of the central portion of the lesion

The diagnosis depends on the isolation of *Erysipelothrix rhusiopathiae*. This can be accomplished by intraperitoneal injection into a white mouse of a suspension of material obtained at biopsy.

VIRAL AND RICKETTSIAL DISEASES

VIRAL DISEASES

The biologic position of the agents classified as viruses is not uniform. The chlamydozoa of psittacosis and lymphogranuloma venereum are gram-negative organisms measuring 400+ millimicrons in size From this the size ranges downward to that of the virus of poliomyelitis, which measures from 8 to 12 millimicrons Generally viruses are organisms of the order Virales They are smaller than most bacteria, are capable of multiplication only within a living susceptible host cell, and pass through standard filters holding back bacteria

An acceptable view of the origin of viruses is that they are degraded descendants of larger pathogenic microbes as suggested by the range of visible forms between bacteria and certain viruses. Rickettsias and the psittacosis viruses resemble bacteria, but their requirements for growth are those of viruses. The smallest viruses have but small resemblance to either rickettsia or bacteria

Concerning the origin of viruses Burnet wrote. "Every virus particle, like any other organism, derives by genetic descent from some similar particle and in its turn possesses the power to produce under appropriate conditions replicas of itself."

It seems that the adaptation of viruses to an intracellular life may be evidence of their loss of the power of chemical synthesis, and therefore they have come to live and to reproduce in an environment in which synthetic chemical power of their own is not necessary.

By means of the electronic microscope it has been observed that bacterial viruses can enter bacteria, where they reproduce themselves in large numbers, later they are

In the animal kingdom the forms which are attacked range from insects to man In many instances the infections caused are limited to one species or type of host, while in others the same viruses affect unrelated hosts In some cases the infections induced are associated with clinical manifestations, in others the infections are apparent in one type of host and inapparent in another.

In some viral infections the manifestations and the pathologic changes are definitely limited to an organ or a system, while others seem to be manifested as generalized, blood-disseminated infections. In this text those viral infections which seem to have mainly organic or systemic manifestations have been described with the organs or systems manifesting the disturbances In this part of the text viral infections which were not conveniently described with a system are discussed.

Smallpox (Variola). Smallpox is a disease of viral origin and always potentially epidemic in nature. However, the disease can be entirely controlled by means of vaccination The lesions of smallpox often heal with scarring

Variola virus is stable and confers a solid immunity.

Immunologic and serologic studies indicate an extremely close relationship between the viruses of variola and vaccinia The presence of common antigens and antibodies, demonstrable by in vitro technics, in variola and vaccinia has been studied in great detail

The characteristic essential lesion of smallpox consists of degeneration of the cells of the deep layers of the epidermis, accompanied by exudation. The exudate increases in amount, and the spaces of the reticulum enlarge until its fibers rupture and the lesion becomes a distended pustule

The subsidence and the healing of the lesions are accomplished by absorption and by drying of the vesicular fluids, and by the regeneration of the epidermis, in the course of which the residual mass of degenerated epithelial cells, leukocytes, and debris is exfoliated.

SYMPTOMS. Twelve days (9 to 20 days) after exposure of a susceptible person to variola virus there are chills, prostration, headache, severe backache, vomiting, and fever up to 103 F (39.4 C) or higher. The aching is deep seated and often most intense in the back and legs. After 3 or 4 days of the fever and aching the temperature recedes and the rash characteristic of smallpox begins

During the course of smallpox, symptoms of pyogenic infections of various types may occur at any time. Terminal bronchopneumonia or bacteremia occurs in practically all cases of fatal smallpox

EXAMINATION The developmental stage is attended by a rash. In some instances this rash resembles both in appearance and distribution that of scarlet fever while in others the rash is macular in form resembling that of measles Both of these skin manifestations tend to be present on glabrous skin over the lower abdomen, medial aspects of the thighs and the lateral thoracic regions.

The macule, 2 to 3 mm in diameter, discrete and fading on pressure, is the common characteristic initial lesion of smallpox The lesions are apparent on the third or the fourth day after the onset of the fever. On the second day after the appearance of the macule the eruption becomes papular. On the third day vesicles form at the apex of the papules. The vesicles are umbilicated On the fifth day the vesicles change to pustules. The fever rises again to 101 to 103 F (38 3 to 39 4 C). This rise of fever attends the development of pustules It lasts but one day.

The swelling about the lesions is attended by pain. The eyes may be swollen shut. Lesions in the mouth and throat may be painful and aphonia is common.

Other lesions of smallpox are the confluent, hemorrhagic (black smallpox); sometimes urticarial lesions are present. Hemorrhagic smallpox is a serious form of the disease which is commoner in those who are strong and robust. On the third or fourth day the usual rash becomes hemorrhagic and ecchymoses appear on the

occur in a subclinical as well as a clinically apparent form in the same type of hos and still others in an apparent form in one type of host and an inapparent one i another

Viral infections are characterized by their ability to confer solid and durab immunity The immunities which follow natural infections are commonly associate with antibodies that appear in the blood. It is generally held that the initial stimulu leading to their formation of antibodies is not entirely responsible for the immunity It seems likely that immunity is due to the virus living and persisting in the tissue and thus serving to keep the immunity alive, for viruses are ordinarily intracellula and antibodies do enter the cells

It has long been believed that well-nourished persons are more resistant to an kind of infections than those who are undernourished or wasted. This belief, how ever, has been challenged repeatedly, particularly in regard to viral infections River has suggested a theory to explain "malnutritional immunity" based on the assump tion that undernourished cells are lacking in biotin or other stored food material necessary for the proliferation of viruses.

Sprunt observed that prolonged fasting may cause a tenfold increase in the nor mal antiviral resistance of rabbits, provided the animals have free access to drinkin water during the fasting period He obtained data which might be construed as proo that a reduction in the amount of local nutritional reserves in dermal tissues prevent viral proliferation That other factors are also operative, however, is indicated from the observation that blebs raised by the intradermal injection of the viral suspen sions subside much more slowly in the fasted animals than in well-nourished controls

Sprunt found that the failure of virus to spread normally in starved animals i due to increased amounts of interstitial fluid, since fasting animals tend to increase the amount of their interstitial fluids if allowed free access to drinking water

Assuming that viral particles are autonomous biologic entities, Rivers postu- lated that depletion of tissue biotin and other nutritional factors might possibly con- tribute to localization of a virus

The laboratory procedures that aid in the diagnosis of viral diseases are highly specialized and not of the kind which can be performed by the ordinary clinical laboratory In some instances a complement-fixing or agglutinating antibody may have been developed. The agglutinating antibody is based on inactivation of virus and the test is therefore partly an in vivo test carried out with susceptible experi- mental hosts. In vitro tests, such as the complement fixation test, are more con- venient and more economical than neutralization tests, but they are not uniformly applicable to the diagnosis of viral diseases A certain minimal amount of viral material must be present in the antigen that is used in such a test, and this is some- thing not easily realized with materials representing all kinds of viral infections However, the complement fixation test, which is the more sensitive of the two in vitro tests, has proved its value in the diagnosis of several viral diseases. In the generally serviceable neutralization test it is important to know that antibodies often do not make their appearance in the patient's blood until late in the disease or after recovery. A large part of the value of these tests lies in the identification of a past infection rather than in that of a current illness In any case it is important to procure a specimen of serum early during the course of a patient's illness, for com- parison with later specimens.

Effective immunization requires the use of active virus. Vaccinia virus, fixed rabies virus and strain 17D yellow fever virus are the three notable examples There are available a few vaccines, consisting of suspensions of inactivated viruses, which will establish immunities of short duration against some viral diseases. Influenza and equine encephalomyelitis are examples

All forms of life, even bacteria, seem to have their special forms of viruses and viral diseases.

varies from one to several dozen and all are situated on the hands and fingers. There is little discomfort, only slight pain and mild itching

According to Kummer there have been reports of 12 cases in which a generalized eruption has occurred. These disseminated lesions are multiform in type, being either umbilicated papules, urticarial wheals, or macules, any of which may become vesicular or hemorrhagic. This generalized outbreak subsides within a week, and the eruption has been considered as being either toxic or produced by hematogenous dissemination of the infection

Examination. The lesions may be seen to develop from erythematous papules which slowly increase in size, becoming firm, elastic, bluish red nodules from 1 to 2 cm. in diameter. The lesions often are surrounded by inflammatory areolas and may be found in various stages of development. Each nodule becomes semiglobular with a central depression; the surface becomes flat, and when the grayish loose epidermal covering is removed, a reddened, granulating base remains. On healing, the entire nodule flattens and softens and the lesion is gone in from 4 to 6 weeks without formation of scars The regional lymph nodes are occasionally enlarged and secondary pyogenic infection with lymphangitis may occur. There is little constitutional reaction except in unusual instances, when the eruption becomes generalized or secondary infection ensues.

Diagnosis. The history of contact with an infected cow, the spontaneous resolution of the nodule, and microscopic examination of the biopsied nodule seem to be the diagnostic criteria.

Measles. Synonyms for measles are morbilli, rubeola, and Masern.

Measles is usually a mild disease of viral origin. The complications of measles which are of bacterial origin are varied and often of a serious nature The disease occurs both sporadically and epidemically but usually in epidemics during the winter and spring months An attack confers a good immunity

The virus is present in the blood and in the nasopharyngeal secretions probably during the whole of the prodromal period and up to 24 or 30 hours following the appearance of rash and it may persist to confer immunity.

Symptoms The incubation period of measles up to the appearance of the exanthem is from 12 to 19 days The average period is 2 weeks The skin rash is preceded by 1 to 5 days of prodromal symptoms consisting of catarrhal manifestations in the upper part of the respiratory tract There are sneezing, coryza, redness of the eyes, cough and fever In some instances a chill occurs and, in most, there are chilly sensations. The characteristic diagnostic lesions are the Koplik or buccal spots when they can be found These appear from 1 to 4 days prior to the onset of rash The fever and cough become steadily worse until the appearance of the rash.

The symptoms of measles are mild and usually insignificant. The symptoms of the frequent complications often are those of serious disease Otitis media, bronchopneumonia and encephalitis are the more common complications, and are due to bacterial invasions, often by the streptococci, pneumococci, or *Hemophilus influenzae*. Appendicitis is a definite but a rare complication of measles.

The symptoms of otitis media and bronchopneumonia occur early, often during the course of the active disease

The symptoms of involvement of the central nervous system (measles encephalitis) appear usually some days after the appearance of the rash, perhaps after the rash has faded The temperature rises again and the patient becomes drowsy and may have convulsions.

Among the 13,037 cases of measles reported to the Philadelphia Health Department by Sawchuk during the 1946 epidemic there were 14 cases of measles encephalitis, a ratio of 1:1,000. Measles encephalitis is suggested by edema, engorgement of the superficial meningeal vessels and prominence of the smaller vessels in the white matter. In an occasional case perivascular staining indicates focal hemorrhages. The convolutions

conjunctivae and there is bleeding from the mucous surfaces. Death may (the fifth or sixth day.

The characteristic of smallpox is that all of the skin lesions in an area ar at the same stage of eruption. The pustules begin to dry and generally arc over by the end of the second week, the scabs dropping off about the en third week A mild leukopenia often occurs during the pre-eruptive stage moderate leukocytosis appears with pustulation.

In hemorrhagic fulminating smallpox, on the second or third day of diffuse, hyperemic rash appears, beginning as small punctate hemorrhage skin. The skin quickly assumes a purplish appearance and there are ecchyn the conjunctivae and sometimes hemorrhages from the mucous membranes. form of the disease there is never a characteristic smallpox eruption over t However, in some instances of hemorrhagic smallpox, bleeding may be delay the rash has appeared, in which case hemorrhage may occur into or betw lesions The blood manifestations in hemorrhagic smallpox are characteriz decrease in polymorphonuclear cells, thrombocytopenia, and a definite l cytosis The changes in the blood resemble those in leukemia.

A case of unrecognized hemorrhagic smallpox may be the means of dis tion and origination of an epidemic of this disease.

Diagnosis The history and the symptoms during the initial stage of sı may suggest influenza or the prodromal phase of many infectious disease eruption of smallpox is usually characteristic. As stated, all the lesions in are in the same stage of eruption at the same time. The cutaneous lesions of sr are more plentiful on the extremities and the face than elsewhere. Severe rhagic forms of smallpox may resemble septicemia, particularly that occurri ing a meningococcal infection The diagnosis of smallpox on clinical evid generally possible The institution of preventive measures cannot wait for re laboratory tests

Reaction to the Paul test, which consists of introduction of the conten vesicle into the scarified cornea of a rabbit, is positive in one half of the The reaction is characterized by a papular keratitis which yields Guarnieri's on examination of the contents of a small umbilicated papule.

A specific precipitin test also has been described but is not in general use

Varioloid. The term varioloid is used to designate a mild variola which in a partially immune person who has been vaccinated successfully a num years previously. The prodromal symptoms are mild. The rash is scanty, bu ceeds through the appointed course of development at a more rapid rate, an or no secondary rise in temperature attends pustulation In some persons m atypical symptoms of the disease may occur and these are epidemiologically

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those recently vaccinated.

The diagnosis of varioloid and variola without exanthem has generally been on epidemiologic evidence In the absence of epidemiologic evidence and suspicion is held it is wise to seek the help of health authorities so that proper nostic laboratory technics can be employed to establish unequivocally the eti of the disease by isolation of virus or demonstration of rise in specific antib during convalescence.

Milkers' Nodules. Milkers' nodules occur in those employed as milkers of having udders crusted or ulcerated with the lesions of cowpox. The disease o during the latter part of the summer. One attack apparently confers immunit seems that the infection enters the skin through abrasions.

Symptoms. The incubation period is from 5 to 7 days. The number of le

monly observed are ocular defects, deafness, cardiac lesions, microcephalus, mental retardation and dental defects. Dental defects are severe in infants belonging to the mothers who had suffered from German measles between the sixth and the ninth weeks of pregnancy, considered to be the "critical" period of dental development. The main dental abnormalities comprised retardation of eruption, hypoplasia of enamel and dental caries. As would be expected the lens of the eye is affected in many of those who have dental malformations

Estimates of percentage involvement of the fetus from maternal rubella during the first three months of pregnancy range from 90 per cent (Australia) to 27 per cent (United States), with a graded decreasing expected anomaly rate from rubella infection in later pregnancy. A woman who contracts rubella during early pregnancy has approximately a 10 1 liability of subsequently being delivered of a congenitally defective child.

Fetal injury is believed to occur as a result of passage of rubella virus through the placenta, thereafter exerting a direct effect on early somatic fetal development. Paradoxically, rubella produces the same result when it occurs and subsides even before conception. Retention of the virus in maternal tissues and its later passage through the placenta to the fetus could account for this as well as the maternal immunity. Other diseases occurring in early pregnancy and in the immediate preconception period, particularly infectious mononucleosis, are also stated to result in congenital defects

The observations of Gregg and associates on the relationship between maternal rubella infection and developmental defects in offspring do not diminish the absolute importance of gene influences, but emphasize the relative importance and scope of environmental factors in human development.

Symptoms. After an incubation period of 10 or 12 days the symptoms commence with sore throat, fever (temperature 99 to 100 F, or 37.2 to 37.8 C), chilliness, headache, coryza and perhaps aching in the back and legs if fever is present

Examination. The throat is somewhat reddened, often there is present irregular areas on the mucous membranes which resemble the skin rash On the second day the skin rash appears on the face, and then it spreads rapidly over the chest and limbs. The eruption consists of erythematous macules which may become slightly elevated and are of varying sizes The rash fades rapidly and is gone in from 3 to 5 days, leaving a moderate brownish desquamation of the involved areas of skin Characteristically there is enlargement of the cervical lymph nodes.

Diagnosis. Rubella often resembles measles and infectious mononucleosis (glandular fever). Differentiation from measles is best established by the absence of Koplik spots and the enlarged cervical nodes. Infectious mononucleosis is characterized by an increase, up to 75 or 85 per cent, of lymphoblastic mononuclear cells in the blood and on the rise in the titer of heterophil antibodies The cervical lymph nodes and the spleen are often palpable in infectious mononucleosis

Pretibial Fever. It seems that the cause of this disease, according to Daniels and Grennan, is a filtrable virus which has been transmitted to guinea pigs and to human beings. The incubation period is from 10 to 15 days.

Biopsies of the cutaneous lesions reveal a diffuse edema and a slight to moderate perivascular infiltration

There may be a mild sore throat, cough and coryza. In some there are frontal headache, postorbital pain, backache, malaise, chills or chilliness and fever. The irregular fever lasts from 4 to 8 days.

On the fourth day of the illness there is present a raised, erythematous eruption of the skin, the lesions being of irregular outline, often 2 to 5 cm in their largest diameter. The eruption is often bilaterally symmetric and limited to the pretibial areas Occasionally the eruption may appear over the entire body. This eruption fades away in 2 days The spleen is palpable. The pulse rate is slow. The leukocyte counts are *equivocal*.

A presumptive diagnosis may be made on the basis of the presence of the fore-

are flattened as a result of edema A cerebellar herniation cone may be present and may account for central cardiorespiratory failure. However, these changes are not specific, since they may be observed in any of the encephalitides.

Neurologic and psychologic examinations were made on 19 of the 34 surviving patients out of 50 patients who include the 14 previously mentioned. Only 2 of the 19 appeared normal. The greatest number of neuromuscular disorders involved the extremities, most of the others involved the cranial nerves Of electro-encephalograms made of 4 of the mentally defective patients, 3 were interpreted as abnormal.

Studies of spinal fluid indicated that a low cell count (fewer than 50 cells per cubic millimeter) in measles encephalitis indicates a grave prognosis.

EXAMINATION Photophobia often is present. On examination the Koplik spots, if definitely manifest, are diagnostic They are usually bilateral and occur at the level of the premolars and around the papilla of the parotid duct; frequently they appear on the mucous membrane of the lower lip. They have a white or bluish white center set on an erythematous base, and are best seen by daylight.

The rash appears on the forehead and behind the ears. It spreads over the neck, body and extremities and usually is fully developed in 2 or 3 days. The first stage is a macular eruption which becomes maculopapular, and the lesions often join to form irregular areas The face usually is swollen and congested and with the catarrhal features has a characteristic appearance The rash may become confluent over the greater part of the body It usually persists for 2 or 3 days after the temperature subsides and then fades rapidly, but instances of longer duration are common. The rash is a hyperemia and disappears on pressure, but in the malignant form of measles it may become red in color Among peculiarities of the rash are the occurrence of numerous miliary vesicles and of petechiae, present occasionally even in cases of moderate severity A sudden recession of the rash may be due to a failing circulation which causes the rash to fade.

At the height of the disease there is often leukopenia until a complication ensues

DIAGNOSIS During an epidemic the diagnosis of measles is easy. The Koplik spots, if they can be seen in the mouth, are diagnostic In sporadic instances of measles, when the progression of the [illegible]
from this. Without Koplik spots and [illegible]
tion from rubella may not be made [illegible]
does not occur in measles Occasionally, under certain circumstances, it may be well to distinguish early smallpox, rubella, scarlet fever and rashes due to drugs from measles.

A detectable diazo substance often occurs in the urine of those who have measles This substance is absent in rubella.

When nervous symptoms are present, the protein and cells of the spinal fluid are increased.

Ford has observed that as high as 65 per cent of the survivors who have had [illegible] and physical impairment.

[illegible] rubella are German measles, rubéola,
[illegible] le
[illegible] n. In adults it is a little more serious. Serious effects are often rendered to the fetus should the mother have the disease during pregnancy

RUBELLA IN HUMAN VOLUNTEERS Experiments carried out on 40 women volunteers demonstrated that typical rubella could be produced by introduction of the virus into the upper part of the respiratory tract The virus can be obtained from nasopharyngeal washings taken on the first day of the rash.

There is evidence that infection provides good immunity for at least 9 years

CONGENITAL DEFECTS. Gregg and his associates presented evidence that maternal rubella infection in early pregnancy appears to be responsible for the frequent development of congenital anomalies in infants subsequently born. The anomalies most com-

SYMPTOMS. In severity the disease varies from an almost symptomless infection to a severe, rapidly fatal one in which death occurs usually within 10 days of onset. Recovery leaves a lifelong immunity. There are no sequelae. The incubation period is 4 to 10 days

There are usually no prodromes The patient becomes ill suddenly. The clinical course in severe instances of the infection is divided into the stages of active congestion and stasis

The onset of the stage of active congestion is acute and characterized by fever, chill, headache, and backache. The temperature rises rapidly to reach its maximum on the first or second day. The initial temperature is continuous and seldom exceeds 103.5 F (39.7 C).

During the stage of congestion the patient is intensely ill and restless. Nausea and vomiting are common. The face is flushed, lips are swollen, and eyes injected. The tongue is bright red A tendency to bleeding may be apparent early. The period of active congestion lasts 3 or 4 days, at the end of which the temperature subsides.

At the onset of the stage of stasis the temperature rises again but seldom reaches its previous maximum The whole aspect of the illness changes during this period The active congestion fades, to be replaced by a venous stasis. The face is no longer swollen, and a dusky pallor replaces the bright red of the first stage. The gums become swollen and spongy and bleed spontaneously or on light pressure. Nausea and vomiting are common. The vomited matter usually contains some altered blood, this is the so-called black vomit. The tendency to hemorrhage is marked; ecchymoses may develop, melena is common

The two stages may coalesce without any drop in temperature. However, in most instances there is a definite rise-fall-rise appearance to the temperature curve

EXAMINATION The appearance of the patient depends on the stage and the severity of the infection. During the stage of congestion the face is intensely reddened, while during the stage of stasis the face is pale.

Prostration may be present and is usually out of proportion to the symptoms The pulse rate is markedly slow in relation to the temperature. The blood pressure is low Jaundice of a mild degree may be present during the second stage of stasis, or it may not appear at all It is more marked in those in whom convalescence is prolonged

Evidence of severe hepatitis and insufficiency may be present and revealed by tests of hepatic insufficiency.

There is a constantly progressive decrease in the number of leukocytes beginning with the onset of the disease The leukopenia reaches its maximum on the fifth or sixth day and is chiefly due to a decrease in the number of neutrophils Leukopenia is characteristic of yellow fever

In the terminal stages formation of urea is diminished. There may be a terminal anuria.

Most deaths occur on the sixth or seventh day, and seldom later than 10 days after onset Complications are not frequent. When recovery occurs, it is rapid and complete.

DIAGNOSIS. During an epidemic, a diagnosis of yellow fever can often be made on the basis of the clinical findings. The laboratory procedures for the establishment of a diagnosis are the isolation of the virus, demonstration of the development of specific antibodies during the course of the disease, and pathologic findings in the liver in fatal instances

The facilities for animal inoculation are usually not available The diagnosis may be established by the examination of two specimens of serum in the protection test. The first is obtained as soon as possible after the onset of the disease and the second during convalescence. If the first specimen is without antibodies, whereas specific antibodies are present in the second, the patient had yellow fever.

going symptoms if influenza and overexposure of the pretibial regions to hot stoves or an open fire are ruled out.

Colorado Tick Fever. This fever is called also mountain fever, tick fever, mountain tick fever, nonexanthematous tick fever, and American mountain fever.

Colorado tick fever is caused by a tick-borne virus. It is a nonexanthematous tick fever as contrasted with Rocky Mountain spotted fever caused by a rickettsia. The virus confers, apparently, a solid immunity since second attacks are unknown.

SYMPTOMS The symptoms commence with chilly sensations and aching of the body Headache, pain in the eyes and lumbar backache attended by anorexia, nausea, vomiting, photophobia, and hyperesthesia of the skin rapidly ensue. The pulse rate increases The temperature rises and is sustained at from 102 to 104 F (38 9 to 40 C) for about 2 days. A remission of the symptoms then occurs, lasting 2 or 3 days during which the patient is somewhat weak. At the end of this period there is usually a recrudescence, and this time the symptoms last for 3 or 4 days. More than one relapse may occur.

The convalescent period of weakness seems unusually long considering the relatively short duration of fever. Complications and death have not been recorded.

EXAMINATION Physical examination reveals only a skin rash and slight hyperemia of the throat and conjunctivae The rest of the findings if any are present are not due to mountain fever. The leukocyte count falls to 2,000 or 3,000 cells per cubic millimeter, the lowest count usually being found during the first relapse. The reduced number of leukocytes is due to the decreased numbers of granulocytes.

DIAGNOSIS. History of exposure to ticks, the recrudescence of the symptoms, and leukopenia suggest a diagnosis of Colorado tick fever Specific diagnostic complement-fixing antigens for Colorado tick fever which give no false positive reactions have been prepared from infected mouse brains The complement-fixing and neutralizing antibodies apparently appear in the blood of human beings about the ninth to the fourteenth day after the onset of the illness.

Yellow Fever. Yellow fever is known also as fièvre jaune, fiebre amarilla, febre amarela, Gelbfieber.

Yellow fever is an acute infection caused by a virus, *Charon evagatus*. Man acquires the infection by the bite of an infected mosquito (see Mosquitoes, Chapter 20). The disease occurs in two main epidemiologic varieties. In the first the virus is transmitted from man to man by certain species of mosquito belonging to the genus *Aedes* of domestic nature, the virus cycle being man—*Aedes aegypti*—man In the second variety the course of a viral cycle involves wild monkeys and forest mosquitoes. Yellow fever, at this moment, is present and is being maintained in large areas of continental South America and Africa.

Yellow fever viral infection gives rise to specific protective antibodies and confers a solid immunity.

VACCINATION The vaccine 17D as prepared by the Rockefeller Institute produces protective antibodies which can be detected after 10 days, and only 2 per cent of serums collected from adults 4 years after vaccination by Fox and Cabral failed to show protective power.

The directions for administration come with the vaccine No local reaction occurs after administration. A general reaction characterized by malaise, fever, and headache may ensue. A severe reaction, often with encephalitic symptoms, is possible but rare. Too, since the vaccine (17D) contains egg protein, an anaphylactic reaction is possible

Characteristically in the most severe instances of yellow fever there is an almost complete destruction of the parenchymatous cells of the liver and associated with these changes are the metabolic disturbances incident to extensive hepatic destruction. The changes in the kidneys account for the marked albuminuria present.

Evidence of erosion and hemorrhage is present in the mucosa at the pyloric end of the stomach. In very few cases is there a complete absence of altered blood in the gastric contents

DIAGNOSIS. Diagnosis is difficult in sporadic, atypical and primary instances of the disease, but is relatively easy during an epidemic.

In order to prove by serologic methods that a given infection was caused by dengue virus, it is necessary to demonstrate that antibodies were either absent or present in low concentration during the acute phase of the illness and developed or increased in amount during convalescence

Phlebotomus Fever (Sandfly Fever). Sandfly fever, pappataci fever, and three-day fever are commonly used names for phlebotomus fever.

The term sandfly fever, popularly used among English-speaking people, has not been accepted in international scientific literature. The term sandfly as used in the United States refers to a different fly belonging to the genus *Culicoides* which has nothing to do with sandfly fever. Pappataci fever, the popular name for the disease in Italy and the Balkans, has also failed to find general acceptance The name phlebotomus fever, which stresses the relationship of the disease to its specific insect vector (the genus *Phlebotomus*), seems acceptable. The fever is of viral etiology.

Experiments on human volunteers residing in phlebotomus-free regions of the United States have shown that a solid immunity to reinfection with the same strain of virus is present for at least 2 years, according to Sabin, after a single experimental attack of the disease The incubation period, which averages from 3 to 4 days, may vary from two and a half to 6 days

SYMPTOMS. After an incubation period of 3 or 4 days the symptoms commence with headache, photophobia, pain in the eyeballs, backache, stiffness in the neck and back, pains in joints and extremities, anorexia, nausea, vomiting, abdominal distress, alteration or loss of taste, sore throat, epistaxis, chills or chilliness and profuse sweating, all of which occur in varying degrees Some patients may have only the general aching and fever. The aching may be severe. There is constipation during the first part of the illness to be followed by diarrhea during convalescence.

The fever ranges upward to 104 F (40 C) within 24 or 48 hours after onset, and the febrile period lasts from 2 to 9 days but usually terminates in 3 or 4 days Fevers of less than 1 day's duration and more than 9 days' duration may occur.

Marked but transitory mental depression occasionally is present during convalescence. Recurrences of the fever and symptoms during convalescence are occasionally observed

EXAMINATION. There are present an erythema of the face and exposed parts of the neck and chest, conjunctival injection which is occasionally limited to the exposed portion of the ocular conjunctivae, tenderness of the eyeballs, and congestion of the fauces, soft palate and posterior pharyngeal wall Urticaria or erythema multiforme may occasionally be observed, but a true rash does not occur

The pulse rate is increased in accordance with height of the fever but returns to normal after the first day or two of fever Bradycardia may be present at the end of the febrile period and during convalescence

On the first day of the disease according to Sabin, Philip and Paul the total leukocyte count is normal There is a relative and absolute decrease in the lymphocytes accompanied by a relative and sometimes absolute increase in the neutrophils which is due to an increase in immature cells During the second or third day of fever, the number of lymphocytes begins to return to normal and for a few days thereafter may constitute from 40 to 65 per cent of the total count. At the same time, the number of neutrophils begins to drop, and the immature cells increase to a point at which they usually outnumber the segmented cells The greatest drop in the total number of leukocytes may not occur until the end of the febrile period or after defervescence, but the marked shift to the left in the neutrophils and changes in the proportions of different types of cells at various stages of the disease are more important for diagnosis than is a single total leukocyte count. The urine is normal.

Dengue (Mosquito-Borne). Dengue has various designations, among which are breakbone fever, dandy fever, denguero, bouquet fever, giraffe fever, polka fever, five-day fever and seven-day fever

Dengue fever is a mosquito-transmitted viral infection. The existence of multiple immunologic types of dengue viruses is known There are at least three immunologic types in Hawaii, New Guinea, India and Japan It seems that all these viruses have at least one common antigen

Neutralizing antibodies for the homologous type of virus have been found in human beings infected by the Hawaiian strain as early as a week after the onset of illness and as late as 2 years. The usual incubation period is from 5 to 8 days, although it may vary from two and a half to 15 days, depending on the amount of virus introduced

SYMPTOMS In about half of those who have dengue fever the onset of symptoms may be gradual with headache, backache, fatigue, stiffness, anorexia, chilliness and malaise A skin rash may precede the fever or become manifested after the fever is present In the rest of the patients the onset is sudden with high fever attended by severe headache, pain behind the eyes, backache, pain in the muscles and joints and chilliness, but rarely a shaking chill. The fever persists for 5 or 6 days and terminates by crisis The temperature rarely exceeds 105 F (40 5 C) Occasionally the temperature will return to normal after 2 or 3 days but a febrile period will return again. The course of the fever may be changed by the administration of aspirin for the aches and pains.

The pulse rate at first increases proportionately to the temperature, but after the first day or two it is slowed An absolute bradycardia may be present during convalescence.

Digestive symptoms such as anorexia, abdominal discomforts, and altered taste sensations are common Diarrhea may be present at the onset, to be followed by constipation during convalescence

There are mild forms of the disease consisting of a febrile illness of from 1 to 3 days In these there is no skin rash Reinfection with a heterologous virus may be encountered in those who have previously had the disease

EXAMINATION On examination there is a flushed appearance of the face, neck and chest; and a punctiform rash, especially over points of friction as at the back of the elbows and front of the knees, may be present early in the disease The bulbar and the palpebral conjunctivae may be injected; the eyes are tender to pressure and painful on movement Photophobia may be obvious Lymph nodes frequently are enlarged, but rarely is the spleen palpable. There may occasionally be sufficient edema about the fingers to interfere with closure of the hand, skin paresthesias are present in some The large joints present no abnormalities even when there is a great deal of pain situated in them

The rash may be macular or maculopapular, commonly appears on the third to fifth day and lasts 3 to 4 days. It commences on the chest, trunk, and abdomen, and spreads to the extremities and face Itching, especially of the palms and soles, is common. Desquamation is rare The rash may not be apparent before the last day of fever or until soon after defervescence. This delayed rash consists of small petechiae over the extensor surfaces of the feet and legs, hands and fingers, and on the buccal mucosa and hard and soft palates. This petechial eruption fades after one to three days, leaving a transitory brownish discoloration.

Leukopenia is present. During the first 24 hours the total number of leukocytes may be normal, but the lymphocytes show an absolute and relative decrease, while the number of neutrophils is increased by the appearance of immature forms As the disease progresses, the total number of leukocytes decreases, sometimes to as few as 1,500 cells per cubic millimeter The lymphocytes toward the end of the febrile period and early in convalescence frequently constitute the major portion of the circulating leukocytes. The leukocyte count returns to normal within a week after defervescence.

persists throughout the illness and may be the chief complaint by the patient Generalized aching and soreness of the ocular muscles are often present. Nosebleed sometimes occurs Prostration and signs of cardiac weakness may be evident from the onset, usually becoming pronounced by the second week of the illness. Constipation may be troublesome throughout the illness The general feature of prostration, tending toward stupor and delirium, becomes graver in the second week. In severe disease with definite cardiac weakness there is a tendency toward development of gangrene of the extremities, more frequently of the toes Mental disturbance is common. This may vary from confusion, disorientation, restlessness, insomnia and irritability to delirium.

In cases of severe involvement which end in recovery there is often a sharp change toward the end of the second week. If the disease is uncomplicated, the temperature falls and the stuporous condition disappears about the fourteenth day. Prostration and cardiac weakness continue for a varying length of time after defervescence, depending to a great extent on the age of the patient, those in the younger age groups recovering more quickly than older persons In instances which proceed to a fatal outcome the prostration and the mental cloudiness increase and coma ensues.

Delirium may be present from the onset During the febrile period or during convalescence, hemiplegia, hemiparesis, aphasia and other focal cerebral symptoms are often present. Jacksonian convulsions or generalized muscular twitchings occur Bulbar palsy is common. Optic neuritis followed by optic atrophy, and neuritis of the facial, auditory and oculomotor nerves are observed. Lesions of the spinal cord causing paraparesis and incontinence are mentioned During convalescence neuritis involving a single nerve or groups of nerves, or of a generalized toxic type, occurs Often the brachial plexus or the sciatic, median, ulnar, axillary or musculocutaneous nerves are affected

Some evidence of involvement of the respiratory system is usually present. This varies from a mild cough, which may never be troublesome, to definite bronchopneumonia The pneumonic process may be the presenting symptom.

Among the complications which may be encountered are bronchopneumonia, parotitis, otitis media, mastoiditis and thrombosis of various veins.

The fatality rate varies in different epidemics In all epidemics the rate is less in children than in adults More than 80 per cent of those more than 50 years of age may succumb In sporadic cases in interepidemic periods the death rate is much lower.

EXAMINATION. Aside from the fever and prostration the most characteristic observation on examination is a skin rash which appears on the fourth to sixth day after onset of the illness It may appear as early as the third day or as late as the ninth day The rash consists of rose red macules and papules. These lesions at first disappear on pressure but become petechial and darker as the disease progresses. In severe involvement coalescence of the lesions occurs The eruption appears first on the medial surfaces of the proximal portions of the arms or on the sides of the thorax and the upper part of the abdomen and spreads to the rest of the thorax, the back and arms and legs, usually being less pronounced on the extremities The palms and the soles may be involved, while the neck and face are seldom included in the area of distribution. The rash becomes brownish as recovery ensues, usually disappearing during defervescence In some cases the remnants of the rash may be discernible for several weeks.

The pulse rate often remains below 120 or even 100. A rate of more than 130 indicates severe involvement with a doubtful prognosis. In some patients there is a decrease in pulse rate (50 to 60) during convalescence, the pulse gradually regaining the normal rate as strength returns. On recovery from a severe attack, shortness

DIAGNOSIS The disease is suspected when outbreaks of an illness with fever of short duration occur during the hot, dry season, especially among the newcomers in countries known to harbor *Phlebotomus papatasii*. In other words, the diagnosis of phlebotomus fever is generally based on clinical and epidemiologic data.

THE RICKETTSIAL DISEASES

Rickettsias are gram-negative microorganisms, coccoid or bacillary, which are parasitic in the arthropods and are highly adapted to their hosts. They sometimes infest man and higher animals, and are grown with difficulty on artificial mediums Those known to be pathogenic for man occur intracellularly in the tissues of their vertebrate and arthropod hosts With the exception of the rickettsia of Q fever, they do not pass filters that retain pathogenic bacteria

A characteristic of this group of diseases, with the exceptions of Q fever and rickettsialpox, is the production in patients of agglutinins for the X strains of *Proteus vulgaris (Bacillus proteus)*. This agglutination of Proteus X (Weil-Felix reaction) has been of great assistance in distinguishing the tsutsugamushi group f[illegible] typhus and spotted fever groups, since with tsutsugamushi agglutinins for [illegible] are typically produced, while the serums of [illegible] OX2 strains There [illegible] immunity, which separate the subdivisions [illegible]

Epidemic Typhus (Louse-Borne Typhus Fever, [illegible] the name epidemic typhus are spotted typhus, petechial fever, jail fever, ship fever, camp fever and exanthematous typhus

Epidemic typhus is an acute infectious disease caused by *Rickettsia prowazekii.* Persons of all ages are susceptible

The disease is transmitted from person to person by body lice. Rickettsias are present in the feces of typhus-infected lice in great numbers, and it is probable that from deposits of such feces they gain entrance to the body through abrasions in the skin. The high morbidity rate among doctors and nurses in epidemics of typhus suggests that the inhalation of dried, infected louse feces or the deposition of air-borne infected material on the mucous membranes may be responsible for some instances of the disease.

The chief epidemiologic characteristics of epidemic typhus are as follows: (1) It occurs among populations disorganized by war, famine or social revolution (2) It occurs first and most commonly in the destitute, in concentration camps and in prisons (3) It is transmitted from person to person through the agency of the body louse (4) The epidemics occur in the winter and spring One attack usually confers immunity which may not be permanent

Often there are present splenic enlargement and bronchopneumonia The essential lesion is focal injury of capillary and precapillary vessels, characterized by endothelial swelling, proliferation and necrosis with thrombosis, and by nodular perivascular exudations Such lesions are most frequent in the skin, heart, great vessels, kidneys, adrenal glands, testes, epididymides and especially the cerebral cortex Splenic hemorrhages and thrombi may be present These findings are essentially the same in all rickettsial infections

SYMPTOMS. The incubation period is between 5 and 15 days, the usual time is 8 to 12 days. The prodromes include 1 or 2 days in which the patient experiences malaise, headache, anorexia and at times nausea In the majority of cases the disease begins abruptly with rapidly rising fever, repeated chills and headaches.

The fever rises steadily, usually reaching its maximum by the end of the first week. Morning remissions of fever occur These remissions may be slight during the second week. The fever falls usually by rapid lysis after about fourteen days, patients who have uncomplicated typhus ordinarily being afebrile by the sixteenth day after the onset

Headache is a prominent symptom, being severe and difficult to relieve It often

where cases of Rocky Mountain spotted fever or of tsutsugamushi may be encountered also. It is practically impossible to make a differential diagnosis prior to the appearance of the rash. Other diseases which typhus resembles are measles, meningococcemia and typhoid fever. Drug rashes also may be confusing

The final diagnosis in the sporadic case depends on the presence of the Weil-Felix reaction The standard Weil-Felix reaction may show some agglutination in dilutions of 1:25 beginning on the fourth day of the illness The important positive diagnostic observation is a rise in the agglutination titer, which may rise to dilutions of 1:30,000 toward the end of the second week of the fever.

The complement fixation test may serve to distinguish typhus from spotted fever and from Q fever. The complement fixation persists for many months.

The rickettsial agglutination test may be employed in the diagnosis of typhus and related fevers.

The injection of endemic typhus blood into a guinea pig causes scrotal swelling and fever.

The case fatality rate is less than 5 per cent in murine typhus, with most of the deaths those of patients more than 45 years of age. The fact that the case fatality rate is much lower in murine typhus than in epidemic typhus has usually been considered to be due to a difference in the virulence of the flea-borne as compared with the louse-borne strains Endemic or murine typhus occurs among populations in which the element of human distress is not paramount

Scrub Typhus (Tsutsugamushi Disease) (Mite-Borne). Scrub typhus is known also as tsutsugamushi, Japanese river fever, flood fever, Kedani mite fever, pseudotyphus of Deli (Sumatra), and coastal fever or Mossman fever of North Queensland (Australia)

Scrub typhus is a typhus-like malady which is widely distributed in the Orient and islands of the Pacific. The disease is acquired on exposure to certain types of vegetation in areas of open country which is overgrown with weeds Ordinarily scrub typhus occurs sporadically or in small outbreaks

The causative organism of scrub typhus is *Rickettsia tsutsugamushi* (*Rickettsia orientalis*). *Rickettsia tsutsugamushi* does not invade the nuclei of mammalian cells, and in this respect it differs from rickettsia of Rocky Mountain spotted fever.

The usual vertebrate host of the virus of scrub typhus in Japan is the field vole *Microtus montebelloi* Certain species of wild rats which are commonly infested by mites probably are the principal reservoirs of the organism of scrub typhus in the Philippine Islands, Formosa, Sumatra and New Guinea

The common vector in Japan is the kedani mite, *Trombicula akamushi* (*Trombicula fletcheri*). In the Philippines, Sumatra, Malaya, India, and Queensland (Australia) *Trombicula deliensis* is thought to be the vector, in New Guinea the rickettsia has been recovered from *Trombicula fletcheri*

PATHOLOGY. Scrub typhus is characterized by a disseminated perivasculitis associated with edema and passive hyperemia These changes are advanced in the heart, lungs, regional lymph nodes, testes and brain Other organs show variable degrees of involvement The necrosis of the skin at the site (eschar) of the primary lesion and the necrosis of the regional lymph nodes are the only histologic evidence of "toxemia" In all cases there is sufficient cardiac involvement to produce impairment of heart function and, in addition, an interstitial pneumonitis of sufficient severity to alter the normal gaseous exchange

SYMPTOMS The incubation period is from 7 to 21 days. The onset of the symptoms may be abrupt, or prodromes may be present Early symptoms usually include chilly sensations or chills, headache, anorexia, orbital pain, and rise of temperature There may be severe malaise, vomiting and prostration. During the first week the patient is alert but during the second week the typhoid state is present There may be partial deafness and generalized hyperesthesia. Coma may be present in the critically ill.

of breath may be present for several weeks. Recovery, once assured, is usually complete and sequelae are absent

In many instances albuminuria is present at the height of the illness. It clears with subsidence of the fever.

Azotemia in epidemic louse-borne typhus is found to occur in more than half of the cases, as indicated by increased concentrations of blood urea and creatinine. The correlation between clinical severity and azotemia is constant. Increased concentration of blood nonprotein nitrogen is present in every instance of the fatal disease. Azotemia appears to be closely associated with excessive destruction of body protein and increased nitrogen excretion, with dehydration and a reduced output of urine in the presence of otherwise normal renal function, and in severe typhus with a sudden rapid fall in blood pressure associated with evidences of renal insufficiency The appearance of renal insufficiency as a complicating condition in the disease is in nearly every instance the earliest indication that the patient's course is severe or may end fatally

The leukocyte count varies from 5,000 to 12,000 or 15,000 per cubic millimeter

The Weil-Felix reaction may become positive during the first week but usually it becomes positive during the second week of illness, reaches its height about the time convalescence is established and disappears rather rapidly. It is advisable to test at least two samples of serum, one taken early in the illness and a second late in the second week. With a sensitive antigen the serums of patients with typhus often reach a titer between 1 10,000 and 1:100,000 The OX19 strain of *Proteus vulgaris* is more commonly agglutinated than OX2 and is the strain customarily employed. The serums of patients who have Rocky Mountain spotted fever also show the Weil-Felix reaction in high titers and consequently this reaction is of no practical value in differentiating between the two diseases Serums from persons suffering from other illnesses not related to the rickettsial diseases may show the Weil-Felix reaction in dilutions as high as 1 320 and occasionally 1 640

The complement fixation can be utilized in the diagnosis of typhus The reaction to this test, with typhus rickettsias used as an antigen, becomes positive during the second week of the disease and may remain positive for many years It is of value in differentiating typhus from Rocky Mountain spotted fever

Endemic Typhus (Murine Typhus, Brill's Disease) (Flea-Borne and Mite-Borne) The difference between the epidemic form and the endemic or murine type is largely epidemiologic, with some variations, not entirely explained, in the immunologic observations

The causative organism of endemic typhus has been named *Rickettsia typhi.*

EPIDEMIOLOGY. The chief epidemiologic characteristics of endemic typhus are as follows. (1) Human cases are associated with rat harbors (2) The disease occurs most commonly among workers in food-handling establishments (3) There is no predominance of cases among the poorer sections of the population (4) Transmission from person to person through contact or by rat fleas has not been observed (5) The peak of prevalence is in late summer and fall

SYMPTOMS. The symptoms of the endemic form of typhus are identical with those of the epidemic form with the exception that on the average they are much less severe. [illegible]

may compri [illegible]

The lab [illegible]

that leukop[illegible]

DIAGNOSIS. Epidemic and murine typhus fever have the same diagnostic requirements

When typhus is present as an epidemic, little difficulty should be experienced in making the diagnosis Sporadic cases, whether of the epidemic or of the endemic form of the disease, give more difficulty. This is true particularly in those regions

patients ill with the disease a rickettsia, *Rickettsia akari*, has been isolated. This strain is antigenically distinct from the organisms causing typhus, tsutsugamushi and Q fever.

SYMPTOMS. The initial lesion appears about one week before any other symptoms are present The patient does not appear ill and continues with a normal intake of food and drink. The onset is sudden, with chills, fever, sweats, backache and lassitude Chills frequently precede the fever. Two or more chills may occur each day. Occasionally there are chilly sensations rather than chills.

The temperature rises rapidly to reach 103 to 104 F (39.4 to 40 C). There are morning remissions. Defervescence is finished in from 2 to 10 days. Sweats follow the chills and the subsidence of the fever during the early morning hours.

Headache is severe. There may be pain back of the eyeballs. Photophobia and occasionally a mild conjunctivitis are present. Backache, myalgias, and general soreness of the muscles are common early in the disease. Lassitude and a feeling of fatigue are common.

EXAMINATION. The initial lesion, or papule, often occurs on an unexposed part of the body. However, it may appear on the neck, the face, or the dorsum of a hand The surrounding skin is normal. As the papule increases in size, the center becomes vesiculated but soon shrinks and becomes a black eschar. The surrounding skin when the eschar has formed is erythematous but without induration. The regional lymph nodes enlarge and may be slightly tender. The initial lesion heals in approximately 3 weeks with formation of a scar.

About 1 week after the appearance of the initial lesion, usually synchronously with the onset of the fever or occasionally from 1 to 6 days later, examination reveals a maculopapular skin rash which is often discrete, but there may be too an accompanying erythematous reaction The papules are firm to the touch and small (2 to 8 mm) Some of the papules become vesicular in 1 to 3 days Drying of the vesicles leaves firm eschars The rash is irregular in distribution over the arms, legs, back, thorax and face The palms and soles are not involved, the mucous membranes rarely The rash is without discomfort and heals without formation of scars

The pulse rate varies with the temperature The spleen rarely is palpable.

Leukocyte counts often reveal a moderate leukopenia The differential smear may confirm the presence of a relative lymphocytosis The leukopenia is gone in about 2 weeks after the onset of fever There is a transient febrile albuminuria Agglutination reactions with Proteus OX19, OX2 and OXK are essentially negative.

DIAGNOSIS. Diagnosis is made by testing with a specific antigen of rickettsialpox or by recovery of an organism possessing the characteristics of a rickettsia from the tissues of a mouse inoculated with blood drawn from a patient who has the disease.

The vesicles in *chickenpox* are superficial, thin and easily broken, while in rickettsialpox they are deep-seated and firm

The pock in the early stage of *smallpox* resembles that of rickettsialpox, but heals with formation of scars. The smallpox rash has a more selective distribution, [illegible] lesion, [illegible] ecchymotic. No initial lesion is present Nearly all patients give a positive agglutination reaction with Proteus OX19 and a positive reaction to the complement fixation test with homologous rickettsial antigens

The lesions of *Rocky Mountain spotted fever* are not so discrete as those of rickettsialpox and they are often ecchymotic and are never vesicular Patients who have Rocky Mountain spotted fever give a positive agglutination reaction with Proteus OX19 or OX2 whereas these reactions are not present in rickettsialpox.

The rash in *scrub typhus* fever is macular or maculopapular and not vesicular. The course of the disease is severer and pulmonary signs are common Serum

The average duration of the fever varies from 3 days to a month. The fe shows morning remissions. There may be afebrile periods lasting as long as 2 t days Defervescence takes place by lysis.

As a rule, the pulse rate rises and falls with the temperature during the f week of illness. In the second and third weeks the pulse tends to become wea and more rapid. The blood pressure usually falls gradually during the second w of illness Circulatory collapse or congestive heart failure may develop

EXAMINATION The rate of the respiration varies from 20 to 30 per minu When pulmonary or cardiovascular complications supervene, the respiratory r may rise to 40 or even 60 per minute

A primary lesion is present in most instances. This lesion begins as an erythe atous macule, becomes a papule, and subsequently ulcerates. The ulcer is shar defined, is surrounded by a red areola, and subsequently a black eschar ensues. T lymph nodes of the drainage area are enlarged The primary lesion appears bef the onset of fever It is most frequently on the ankles and lower parts of the l or on the thighs. Usually this lesion is single, but two primary lesions may oc on different parts of the body

There are redness of the throat and unproductive cough in the early stage scrub typhus Passive congestion of the bases of the lungs is present Bronchitis bronchopneumonia is common

A rash usually develops between the fourth and the seventh day It may app first on the sides of the chest and abdomen. It sometimes appears on the fa rarely on the palms and soles The rash is maculopapular at first. In the beginni the color disappears on pressure The lesions are often discrete and rare petechial

The superficial lymph nodes are enlarged. Greater enlargement, pain, a sensitiveness may be found in the group of nodes draining the region in which t primary lesion is situated than in other nodes.

The spleen is palpable and tender

Subconjunctival hemorrhage may occur Edema of the optic disk and of t retina may be observed during the second and third weeks Retinal hemorrhag occur rarely

The urine usually contains some albumin Slight anemia is present In the ear stages of illness the leukocyte count is normal. Later there may be a slight increa of polymorphonuclear cells followed by an absolute lymphocytosis which persis during convalescence. The leukocyte count varies from 1,500 to 19,500 per cub millimeter of blood The lymphocytes range above 40 per cent

DIAGNOSIS Scrub typhus differs from typhus in that the eruption is mor frequently absent and seldom becomes petechial A presumptive diagnosis ca often be made by finding the characteristic primary lesion and a regional or genera adenopathy.

Reaction to the Weil-Felix test becomes positive with Proteus OXK about th twelfth or fourteenth day of illness in most cases The causative organism, Rick ettsia tsutsugamushi, can be recovered readily from the blood of patients durin the acute stage of the disease by the intraperitoneal inoculation of 0.2 to 0.3 ml of blood in white mice When the reaction is positive, both of these laborator procedures establish the diagnosis, but the disease is not excluded by a negative Weil-Felix reaction with Proteus OXK The complement fixation test gives reac tions which are specific.

In mild instances of scrub typhus prognosis is excellent When cyanosis or bronchopneumonia appears, the outlook is grave.

Rickettsialpox (Mite-Borne). Rickettsialpox, also called Kew Garden fever, is an acute, febrile disease occurring in areas infested with mice and rats. Because of some similarity to chickenpox the name rickettsialpox has been assi ned From

The Weil-Felix reaction gives no aid in differentiating spotted fever from typhus. In a large number of cases it has been noted that agglutinins for Proteus OX2 occur more frequently in the serums of patients with spotted fever than in those of patients with typhus, but since they do occur in some of the latter the stated difference is of no help in the individual case. When agglutinins for both strains are present, those for OX19 are usually higher than those for OX2. The agglutinins for OX19 usually appear toward the end of the second week of the disease At times they are delayed until early convalescence. In some proved cases of spotted fever no agglutinins for Proteus X are produced The curve of agglutinins in its rise and fall is similar to that seen in typhus. As in typhus, it has been found that complement fixation with the rickettsias of spotted fever used as an antigen becomes positive in the second week of illness.

DIAGNOSIS. The diagnosis depends on the laboratory findings as enumerated Generally, spotted fever differs from typhus chiefly in two respects: (1) In spotted fever the rash appears first on the extremities and spreads centripetally. (2) Gangrene of the genitalia is common in spotted fever but is very rare, if it occurs at all, in typhus. Cutaneous and subcutaneous hemorrhages seem to be commoner in spotted fever than in typhus

In typhus fever the pulse rate usually rises and falls with the fever and is proportional to the elevation of temperature. In spotted fever the pulse may be relatively slow early in the disease or throughout the course of the fever. In typhus fever the eruption very rarely occurs on the face.

A vaccine made from infected ticks for use against spotted fever was elaborated and is prepared by the United States Public Health Service at Hamilton, Montana. There is no good evidence that the vaccine is of value after the infection has been acquired, nor is it of any value in treatment It may offer some protection during sojourn in infested areas. According to reports, chemotherapy has given good response in some instances

Boutonneuse (Tick-Borne) Synonymous names for boutonneuse are Marseilles fever, fièvre exanthématique, and escarro-nodulaire

Boutonneuse is caused by *Rickettsia conorii* and is closely related to Rocky Mountain spotted fever. It has an extensive distribution in Rumania, Portugal and the countries bordering the Mediterranean.

The infection is transmitted by the brown dog tick *Rhipicephalus sanguineus.*

SYMPTOMS. The incubation period is 5 to 7 days, although in occasional cases it may be as long as 18 days

As in other rickettsial infections, the onset is usually abrupt, with fever and repeated chills or chilliness The temperature rises rapidly and may reach 104 F (40 C) in a few hours Headache and pain in the muscles and the joints are common complaints. Prostration is usually not a prominent feature of this disease The febrile period is from 8 to 14 days, defervescence taking place by rapid lysis

Insomnia is common throughout the febrile period As the disease is seen in Marseilles and Italy, mental disturbance is less severe than in other rickettsial infections, although patients who have severe involvement may show moderate delirium The case fatality rate is low, being less than 3 per cent

EXAMINATION A papular or maculopapular rash appears on the second to fourth day of illness It begins on the trunk, legs and arms and extends rapidly over the entire body, usually appearing on the face last The palms and the soles are commonly involved The rash may be less pronounced on the abdomen than elsewhere It may be found on the soft palate as small round red spots which persist only a few days

The individual lesions comprising the rash may become hemorrhagic, especially those on the legs, but there is little tendency to coalescence The rash usually disappears with convalescence.

Frequently a small ulcer about 2 to 5 mm in diameter, showing a black necrotic center surrounded by a red areola, is found at the onset of illness This has been

agglutination with Proteus OXK occurs about the second week in a majority of cases. Specific complement fixation antigens are also available for differentiation

The rash in *boutonneuse fever* is papular or maculopapular and frequently involves the palms and soles. Serum agglutination of Proteus OX19 occurs late in the disease or in the convalescent stage. There is a history of a tick bite.

Rocky Mountain Spotted Fever (Tick-Borne) The causative agent is *Rickettsia rickettsii (Dermacentroxenus rickettsi)*

The usual vectors for the transmission to man of Rocky Mountain spotted fever are the wood tick of the Northwest (*Dermacentor andersoni*) and *Amblyomma americanum* and the American dog tick (*Dermacentor variabilis*).

Rocky Mountain spotted fever is a severe rickettsial disease which occurs when a human being is bitten by an infected tick The important endemic foci in the United States are Wyoming, Montana, Colorado and the Southern Atlantic states (Virginia, Maryland and North Carolina) In the West the majority of cases appear between April and June, and in the East, during July and August A greater number of victims of spotted fever show focal lesions in the midbrain, pons, medulla and cerebellum than do those of typhus

SYMPTOMS. The incubation period is from 2 days to 12 days The average is about 1 week

The symptoms of Rocky Mountain spotted fever resemble those of epidemic typhus fever There are prodromes consisting of loss of appetite, listlessness and headache The onset is usually sudden, with a chill or chilly sensations and rapidly rising fever. Prostration is usually pronounced In the severer type of the disease nosebleed may occur early. Soreness of the muscles and the joints is commonly present. The temperature rises rapidly, reaching its highest point usually in the second week. Morning remissions of 1 to 3 F occur. The termination of fever is by rapid lysis occurring usually about the twenty-first day, although patients who have mild disease may be afebrile before the end of the second week

Nervous and mental symptoms are common. restlessness, insomnia, disorientation and in severe instances delirium In fatal spotted fever, coma usually precedes death, which occurs about the end of the second week.

Convalescence of patients who have severe involvement is likely to be slow and may be complicated by visual disturbances, deafness or mental confusion Although recovery may be delayed, it is usually complete. The case fatality rate, as in typhus, varies directly with age, it is about 1 in every 5 who have this fever

EXAMINATION The most characteristic finding on physical examination is the rash. This appears between the second and fifth days, usually on the third or the fourth day The rash may be preceded by a suggestive mottling of the skin, and this resembles the early rash of measles. This introductory rash disappears in a few hours to be replaced by the maculopapular lesions The lesions are erythematous at first and become fainter, almost disappearing during the morning remissions of fever early in the disease They become more distinct each day until they are definitely petechial in all but the mildest forms of infection. In severe involvement the spots become deep red or purplish and confluent Necrosis may develop. The rash usually persists throughout the febrile period and into convalescence, becoming brownish Often a branny desquamation occurs over the areas where the rash was thickest. The site of first appearance and the spread and final distribution of the rash are important in the diagnosis of the disease. Usually the rash appears first on the wrists and the ankles, spreading rapidly in the first 24 to 48 hours to the back, then to the arms, the legs and the chest, and last to the abdomen, where it is least pronounced. The palms and the soles are frequently involved, often the face and occasionally even the scalp

The leukocyte count is increased in cases of Rocky Mountain spotted fever, usually being about 12,000 per cubic millimeter, although it may be as high as 30,000.

The Weil-Felix reaction gives no aid in differentiating spotted fever from typhus In a large number of cases it has been noted that agglutinins for Proteus OX2 occur more frequently in the serums of patients with spotted fever than in those of patients with typhus, but since they do occur in some of the latter the stated difference is of no help in the individual case. When agglutinins for both strains are present, those for OX19 are usually higher than those for OX2. The agglutinins for OX19 usually appear toward the end of the second week of the disease. At times they are delayed until early convalescence. In some proved cases of spotted fever no agglutinins for Proteus X are produced. The curve of agglutinins in its rise and fall is similar to that seen in typhus. As in typhus, it has been found that complement fixation with the rickettsias of spotted fever used as an antigen becomes positive in the second week of illness.

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Insomnia is common throughout the febrile period As the disease is seen in Marseilles and Italy, mental disturbance is less severe than in other rickettsial infections, although patients who have severe involvement may show moderate delirium. The case fatality rate is low, being less than 3 per cent.

EXAMINATION A papular or maculopapular rash appears on the second to fourth day of illness It begins on the trunk, legs and arms and extends rapidly over the entire body, usually appearing on the face last. The palms and the soles are commonly involved The rash may be less pronounced on the abdomen than elsewhere. It may be found on the soft palate as small round red spots which persist only a few days.

The individual lesions comprising the rash may become hemorrhagic, especially those on the legs, but there is little tendency to coalescence. The rash usually disappears with convalescence

Frequently a small ulcer about 2 to 5 mm in diameter, showing a black necrotic center surrounded by a red areola, is found at the onset of illness. This has been

named tache noire (black spot) and is similar in appearance to the ulcer often seen in *tsutsugamushi* The *tache noire* may be found on any part of the body, usually on a part covered by clothing, this is supposed to be the site of the infecting tick bite. Sometimes the regional lymph nodes become enlarged and tender.

DIAGNOSIS. The Weil-Felix reaction with the OX19 strain of *Proteus vulgaris* used as an antigen becomes positive late in the disease.

There is no specific treatment for boutonneuse, and no vaccine is available at present.

Q Fever (Air-Borne and Food-Borne). The cause of Q fever is *Coxiella burnetii* (*Rickettsia burnetii*), and ticks infected with this organism have been found in many parts of the United States. The epidemiologic investigations of the occurrence of Q fever have revealed a close association with animal life, such as pigeons, rats, mice and cattle. Contamination of the environment with excreta or secreta of infected animals has been suggested as a means of dissemination of the rickettsia from animal to man. Evidence concerning the portal of entry is not conclusive but suggests that human infection may occur through ingestion or inhalation of the rickettsia

A minimal incubation period of 13 days is postulated, with a mean which is probably somewhat longer. The exact course of infection and mode of transmission cannot be ascertained, but the epidemiologic data point to the existence of an extra-human source and an intermediary host

SYMPTOMS. The onset may be sudden; many patients are able to state the hour at which they became ill. As a rule the onset is accompanied by chilly sensations, sweats, a feeling of general malaise with weakness and sometimes muscle aches, frontal headache and anorexia Thoracic pain is common, and this varies from vague aching to a pleuritic type of pain. Occasionally gastrointestinal symptoms consisting of diarrhea or mild abdominal cramps are present.

In other patients the onset of the symptoms commences with headache which is not severe Fever and chills and chilliness may be present, though a real chill is rare Muscle aches and pains and symptoms referable to the respiratory tract are common, as are mild gastrointestinal symptoms.

The average period of illness is 4 days In 1 in 10 the illness lasts longer than a week. In all patients the course of the disease is mild There is little prostration, and the patients are not any more incapacitated than they would be with a mild fever from any cause

EXAMINATION. The results of general examination are negative except for the fever.

DIAGNOSIS Specific diagnosis can be established only by special laboratory procedures Tests by complement fixation and agglutinin absorption are required.

Trench Fever (Louse-Borne). Trench fever, also known as five-day fever, Volhynia fever, His-Werner disease, skin fever and shank fever, is a febrile disease transmitted to man by the body louse Extracellular rickettsias have been found in lice fed on patients with the disease and are present in the feces of such lice

The incubation period varies from 5 to 20 days The onset is sudden with headache and pain in the legs, most noticeable in the region of the tibia There is a sudden onset of fever which may last 1 week Three or four episodes of fever of a few days' duration are common.

A macular rash is present at the height of the fever in the majority of cases Occasionally papules will be present. This rash may occur as early as the second day of the initial attack of fever or during one of the relapses. It is most commonly observed on the trunk and may disappear in 24 hours.

There is no report of agglutination of any of the X strains of *Proteus vulgaris* by serums from these patients.

Death or permanent sequelae do not occur as the result of trench fever.

The Spirochaetaceae are a family of the order Spirochaetales containing protozoon-like organisms which occur in the form of coarse flexuous spirals This family includes the genera *Spirochaeta*, *Saprospira*, and *Cristispira*

The genus *Spirochaeta* embraces slender, nonflagellated, wavy, nonpathogenic forms which inhabit sewage and foul water.

Several species of organisms which were formerly termed *Spirochaeta* have been transferred to other genera. Their names and their present classification follow *Spirochaeta carteri*, *Spirochaeta duttoni*, *Spirochaeta gallinarum* (*Borrelia anserina*), *Spirochaeta novyi*, *Spirochaeta obermeieri* (*Spirochaeta recurrentis*), *Spirochaeta refringens*, *Spirochaeta theileri* and *Spirochaeta vincentii*, retaining their original species names, are now with the genus *Borrelia;* for example, *Spirochaeta vincenti* is now *Borrelia vincenti* Likewise *Spirochaeta hebdomadis* and *Spirochaeta icterohaemorrhagiae* are now *Leptospira*, losing their spirochetal cognomen *Spirochaeta icteroides* is now *Leptospira interrogans*. Again, *Spirochaeta morsus muris* is now *Spirillum minus*. *Spirochaeta pallida* is now *Treponema pallidum*, and *Spirochaeta pertenuis* is *Treponema pertenue*.

The Treponemataceae are a family of the order Spirochaetales containing protozoonlike organisms which occur in the form of coarse or slender spirals The family includes both genera nonpathogenic to man and genera pathogenic to man.

Three genera which are pathogenic for man are (1) *Treponema*, of which *Treponema pallidum* is the cause of syphilis; *Treponema pertenue*, the cause of yaws; and *Treponema carateum*, the cause of pinta; (2) *Borrelia*, several species of which cause relapsing fever, and (3) *Leptospira*, several species of which cause spirochetal jaundice (Weil's disease)

Treponema pallidum is present in the blood in syphilis, especially during the primary and secondary stages, but is not detectable except by the inoculation of the testicles of rabbits with blood. This diagnostic method does not prove to be a practical diagnostic procedure. Spirochetemia occurs frequently and early in relapsing fever. For this reason examinations of fresh blood for the spirochetes by darkfield microscopy, or examinations of stained smears (preferred), as well as the inoculation of mice, are valuable diagnostic aids Likewise in rat-bite fever darkfield examinations of fresh blood may reveal the presence of *Spirillum minus* but since errors may occur due to artefacts, examinations of stained smears are preferred, although for diagnostic purposes they are inferior to intraperitoneal inoculation of mice or guinea pigs with blood, exudate or tissue removed from the primary lesion or material aspirated from lymph nodes Infection of the blood with the fusiform bacilli and spirochetes associated with Vincent's angina, gingivitis and gingivostomatitis (fusospirochetosis) is rare. Nevertheless, metastatic lesions occur and positive blood cultures, if made and cultivated under anaerobic methods, may be obtained

In leptospirosis of infectious jaundice (Weil's disease), *Leptospira icterohaemorrhagiae* can be found by darkfield examinations of the blood, but the procedure is not recommended for diagnostic purposes. Cultures of the blood are more valuable. However, most valuable for diagnosis is the inoculation of guinea pigs with infected blood and urine Serum agglutination tests are the most practical and reliable for diagnostic purposes, in all forms of the disease.

The Treponemas. The treponemas are extremely slender spiral rods which are motile by means of flexuous bending of the body

***Treponema pallidum* and Syphilis.** *Treponema pallidum* is actively motile, rotating on its long axis at a fairly constant speed This treponema is difficult to stain with the ordinary aniline dyes, but reduces silver nitrate to form a black surface deposit which permits its demonstration in tissues. It has been suggested that *Treponema pallidum* may have a cyclic development, in one phase of which it is present in a granular and microscopically invisible form, but this is probably a distortion of facts by protagonists of certain poorly conceived theories

IMMUNITY Immunity exists in a syphilitic patient, but it is never at any stage of the disease more than relative. It is doubtful that any degree of immunity is conferred by having had this disease. Intensive treatment of early syphilis with arsenic, mercury, iodides and such drugs may cure the patient if administered in adequate doses, but such treatment simultaneously abolishes all immunity which has developed The effects of penicillin treatment on immunity have not been determined. If antisyphilitic therapy is inadequate, the patient's natural defensive mechanism is seriously impaired. This means, as Chesney has stressed, that the patient is left both without cure and without defense, a situation often leading to neurorecurrences, therapy-resistant cutaneous relapses and precocious tertiarism A patient may be completely cured and yet remain refractory to natural reinfection Even in patients treated early, reinfection does not necessarily mean that the first infection has been completely eradicated, theoretically, at least, superinfection may have occurred because, as Moore pointed out, adequate methods of differentiating between the two are not available.

Urbach and Beerman stated that *immunity in syphilis is a special aspect of allergic* hypersensitiveness The entire course of syphilis may be explained on the basis of allergy The reaction of the organism to reinfection also suggests an allergic mechanism Chesney expressed the belief that the destructive character of tertiary lesions is due to hyperreacting defensive mechanisms of the patient toward the spirochetes, and thus *minimal numbers of spirochetes are capable of initiating tissue reaction and thus increasing* the injury by the infection Attempts to determine the presence of the allergic state, mechanism of the defensive reaction, existence of antibodies, the relationship of the positive serologic reaction to the organism's capacity to produce antibodies against spirochetes, and attempts to induce active or passive immunization against syphilis have failed

Agglutinins, precipitins and complement-fixing antibodies are present only in a sufficient concentration to combine with a lipid present in the tissue to give positive results of complement fixation and flocculation tests with aqueous suspensions of that lipid In ancient syphilitic infection these lipid antibodies often disappear from the serum but may still remain in the spinal fluid

The symptoms, the physical findings, and the diagnosis of syphilis of the various organs and systems are described in special sections of this text

THE CHANCRE The infection caused by *Treponema pallidum* is transmitted by intimate human contacts such as coitus That is, 9 of every 10 primary lesions are situated on the genitalia, while 1 of every 10 has an extragenital situation. All primary lesions are on mucous membranes or on the thin infolding skin about the genital orifices, for it is doubtful that the organism can penetrate the intact glabrous skin Extragenital lesions are usually on a lip, in the mouth, and rarely on a tonsil The incubation period for chancre development is from 10 to 90 days.

The hard chancre is the primary lesion of syphilis Its appearance depends on its stage of development and secondary infection which may be present A chancre commences as a reddened, nontender papule Four or five days later it is indurated. Induration progresses, but if there is no trauma or manifest secondary bacterial infection, erosion does not necessarily ensue However, almost always there are enough trauma and infection so that by the end of 2 or 3 weeks there is a circumscribed, round or oval, raised, eroded, moist, cyanotic, hard, indolent lesion surrounded *by an inflamed border The lesion bleeds easily on slight trauma* If the lesion is situated on the uterine cervix, profuse exsanguinating hemorrhages may occur.

Regional, and soon a generalized, lymph node enlargement ensue

In from 2 to 8 weeks the lesion heals If there has been no ulceration, a scar *is not present.* The usual ulcerating chancre heals with scar formation. The scar of a healed chancre may be of diagnostic importance for the rest of the life of the patient.

SECONDARY LESIONS. Two to 12 weeks after the appearance of the chancre a noticeable, generalized cutaneous rash often appears (secondary syphilis). This

stage of syphilis, characterized by a cutaneous eruption, may also involve the mucous membranes, eyes, osseous system, and the central nervous system. This so-called secondary syphilis results from a generalized dissemination of the organisms and their multiplication. The secondary lesions, as has been mentioned, indicate the development of antibodies and an allergic response to the products of infection.

The secondary lesions of the mucous membranes in syphilis occur on the buccal surfaces as grayish indistinct lesions The secondary macular cutaneous lesions appear on the palmar surfaces of the hands, on the wrists, and on the medial aspects of the knees and legs below the knees. The papular eruption is most commonly observed on the face, trunk, and abdomen These lesions are reddish brown. These have been described more fully in Chapter 8

More important here are the general symptoms consisting of lassitude, and pains through the body, more especially affecting the large bones near their joints. Headaches may be more severe at night than in the daytime The temperature may rise to 100 or 101 F (37 8 to 38.3 C) during the evening. In susceptible persons these symptoms may be severe enough to confine the patient to the bed.

The subsequent course of syphilis after the secondary stage depends on the particular tissue involved. The *Treponema pallidum* may involve almost any of the body tissues However, a syphilitic infection does not necessarily mean that generalized or localized disease will ever occur Twenty-five per cent of those who have syphilis recover spontaneously, another 25 per cent do not recover, but the disease remains without clinical manifestations. Of the remaining one half who have been infected with syphilis, an indefinite number are cured by adequate treatment. No percentage can be assigned to those who are cured by treatment In those left uncured by treatment, syphilis develops which becomes manifest. Some recover after inadequate treatment. There is left, then, an indefinite number in whom there develop complications varying in severity and prognosis. The less susceptible persons have benign gummas In the more susceptible, there develops serious disease of either the cardiovascular system or the central nervous system

Diagnosis of Syphilis The diagnosis is established by (1) clinical manifestations and observations, (2) the demonstration of *Treponema pallidum,* usually by darkfield examination of the exudate from an open or abraded primary or secondary lesion and (3) serologic changes in the blood and spinal fluid

The routine diagnostic employment of the darkfield examination is not practical for general use.

The serologic diagnosis of syphilis is based on the demonstration in the serum or in the spinal fluid of the lipid substance which combines to give positive complement fixation, and on flocculation tests In practice many complement fixation and flocculation tests of serum have been developed for the diagnosis of syphilis, all of which use as antigen suspensions of tissue lipids in an aqueous medium. In both the Wassermann and flocculation tests the degree of positivity may be expressed as the highest dilution of serum which gives a positive result Alternatively, in the Wassermann test it may be expressed as the amount of complement which can be fixed under standard conditions by a given amount of serum However, the reactions are reported from the laboratory as +− doubtful, + weakly positive, ++ and +++ moderately positive and ++++ strongly positive

The lipid substance demonstrated in the serum of syphilitic patients does not pass into the spinal fluid In patients who have syphilis of the central nervous system, the antibody apparently is elaborated locally and appears in the spinal fluid, sometimes in dilution titers exceeding that of the blood. A positive result of complement fixation or flocculation test in the spinal fluid is indicative of involvement of the central nervous system The Wassermann or flocculation titer of the fluid, associated with its cell content and protein content, and their response to antisyphilitic treatment, provide information of diagnostic and prognostic value

INTERPRETATION OF SEROLOGIC REACTIONS When diseases giving biologic nonspecific or falsely positive reactions are excluded, *positive serologic reactions* are almost invariably indicative of *syphilis, yaws, pinta or bejel.*

The incidence of positive reactions in the different stages of syphilis varies according to the sensitivity of the test or tests employed. The incidence in primary syphilis is about 75 per cent, in untreated secondary syphilis the incidence is 100 per cent; in early latent syphilis, late latent syphilis and cardiovascular syphilis about 85 per cent; in neurosyphilis about 95 per cent and in congenital syphilis 90 to 100 per cent It is much better to conduct the test 2 weeks after birth than to try to use cord blood for the test

The interpretation of *unexpectedly positive reactions*, especially when the tests are weakly positive or doubtful, or when one test gives a positive and another a negative reaction, or when the reactions fluctuate from positive or negative, or the reverse, may be difficult. If the patient is known to have syphilis, the results are to be regarded as positive If syphilis is not suspected clinically, the test is repeated one or more times In the meantime, to avoid iatrogenic syphilis the patient is not told of the serologic reaction. However, to disregard a positive reaction because it was unexpected is reprehensible

When doubtful reactions are recorded, the patient should not be informed of the results until a final conclusion is reached on the basis of history, physical examination and a repetition of the tests in the same and in another laboratory.

Falsely positive reactions due to errors in technic occur more frequently in flocculation tests than in complement fixation tests However, there are not more than 1 per cent falsely positive reactions, and these can be checked by repeating the serologic tests

A more important consideration concerns those biologic nonspecific or falsely positive reactions that may occur with the serums of normal persons. The serums of normal persons may contain reagin or reagin-like substances capable of giving falsely positive flocculation reactions

It is known that positive complement fixation and flocculation reactions often occur in cases of yaws, pinta and bejel, since these diseases are caused by spirochetes closely related to *Treponema pallidum*. Positive reactions may occur in the relapsing fevers, rat-bite fever due to *Spirillum minus* and the leptospiroses, but the incidence is variable

In leprosy of all types and in malaria falsely positive complement fixation and flocculation reactions may be observed

Positive serologic reactions are occasionally observed in vaccinia and vaccinoid, infectious mononucleosis, viral (atypical) pneumonia including viral pharyngitis and bronchitis, and other infections of the upper part of the respiratory tract. Positive reactions occur in trypanosomiasis and especially in Chagas' disease, lupus erythematosus, epidemic and murine typhus fever, subacute bacterial endocarditis or any febrile state

It is justifiable to suspect positive reactions as being false or nonspecific when *occurring in virgin girls or women with no history of what may have been an extragenital chancre* as well as, sometimes, in the case of boys or men who deny sexual exposure, also in patients thought to be truthful, and who in the past have had negative reactions and deny sexual exposure, likewise in married persons who, since marriage, have had one or more negative reactions preceding the positive one ... marital partners are found seronegative In a final analysis the conclu-

infectious mononucleosis, along with repeated serologic ...
tories and by different procedures, including quantitative tests over a period of at least 3 to 6 months. If persistently positive reactions are observed in the absence of

any of the foregoing enumerated conditions, it is advisable to regard chronic asymptomatic syphilis as present and to institute treatment for this disease. Examinations of spinal fluid are also helpful in the sense that positive reactions would be indicative of the presence of syphilis; negative reactions, however, would not exclude syphilis.

Positive serologic reactions may occur in well-treated syphilitic individuals after a period of negativity. These *serologic relapses* are interpreted in practice as indicative of renewed activity of persistent foci of infection or a reinfection and indicate the resumption of treatment in order to prevent clinical relapse or progression of the disease.

Seroresistance, Wassermann-fastness, is failure of the titer to fall satisfactorily after treatment, that is, persistently positive serologic reactions despite treatment It is present in late syphilis, in which the serologic reactions fluctuate back and forth from negative to positive.

Wassermann-fastness is encountered more frequently at present than when the Wassermann test alone was employed. The present complement fixation and flocculation tests are more sensitive. The consensus is to the effect that seroresistance is due to the production of reagin in persistent foci of syphilitic infection Relapses of symptoms are 4 times more frequent among seroresistant than among seronegative persons. Seroresistant persons often have infection of the central nervous system.

Falsely negative reactions can occur in late syphilis in both the latent and active stages. In late untreated primary syphilis, falsely negative reactions may occur, although they are almost invariably absent in untreated secondary syphilis. [illegible] may occur in serums of cases of cardiovascular [illegible] venile and acquired paresis. And while positive [illegible] with manifest lesions of syphilis, falsely negative reactions may occur in older children. The serologic tests frequently fail to give positive reactions in late congenital syphilis even in the presence of stigmas A negative reaction and even repeatedly negative reactions should not be permitted to influence clinical judgment

Examinations of Spinal Fluid The cerebrospinal fluid may give positive reactions in both acquired and congenital syphilis when the serum reacts negatively. Whenever late syphilis is suspected, it is generally advisable to conduct an examination of the cerebrospinal fluid in the diagnostic survey, including not only the complement fixation or flocculation tests but a total cell count, a test for increase of protein and a colloidal gold or mastic test. Syphilis cannot be regarded as cured on the basis of negative serologic reactions without 1 or 2 complete examinations of the cerebrospinal fluid

The spinal fluid in acute syphilitic meningitis has a pressure of from 150 to 300 mm of water. It is clear or opalescent and the cell count ranges up to 2,000 lymphocytes. The globulin is increased and there are 45 to 450 mg of protein per 100 ml. The concentration of sugar is from 18 to 75 mg per 100 ml. of spinal fluid The Wassermann reaction is positive in the spinal fluid in one half of the cases

In juvenile paresis the spinal fluid is under normal pressure and is clear, lymphocytes vary from 10 to 150, globulin is increased and there is a normal sugar content. The Wassermann test is positive and the gold curve is paretic (5555432000).

In adult general paresis the findings are, for practical purposes, the same as those present in juvenile paresis. These are zone one reactions

In tabes dorsalis the spinal fluid findings are the same as those of paresis except the gold curve is tabetic. Characteristically there is a second zone reaction (1123210000).

In syphilitic meningitis there is a third zone reaction (0001234530).

Premarital Examination for Syphilis Laws have now been enacted in some 30 or more states requiring for issuance of a marriage license a clinical examination and a laboratory test for syphilis and certification by the examining physi-

cian that the applicants for license do not have syphilis in a stage that is actually or potentially communicable.

The law is not intended to prevent permanently the marriage of persons who have syphilis, but only to delay the marriage of those who have communicable or potentially communicable syphilis until the disease has been rendered permanently noninfectious.

The examining physician performs the necessary examinations to determine whether the candidate for marriage has syphilis, and if so, whether the disease is in a stage or form that is or may become communicable. Whether the candidate for marriage has syphilis or not is obtained from the history and clinical examination and confirmed by serologic tests for syphilis.

A negative blood serologic reaction for syphilis does not rule out the possibility of syphilis The serologic changes in the blood may be negative in the presence of the early stage of a chancre. However, a single positive serologic reaction, unsupported by clinical evidence or history of syphilis, should not be interpreted as diagnostic of syphilis A positive reaction to a serologic test is not evidence of communicability of the disease The blood reaction may be and often is positive though the patient is permanently noninfectious.

If a candidate for marriage has syphilis, the physician is obligated to form an opinion as to whether or not the condition is actually or potentially communicable.

Syphilis presenting open lesions, or an early stage of the infection even though there are no open lesions, if untreated, must be considered potentially infectious. Candidates who have late syphilis are not likely to transmit the disease to a marital partner For purposes of certification for marriage, congenital syphilis in a candidate may be considered noncommunicable.

A candidate for marriage who has a seropositive blood reaction should have an examination of the spinal fluid If a candidate for marriage has neurosyphilis, the decision whether or not marriage should be permitted is a difficult one to make. A state law that requires postponement of marriage of persons who have communicable syphilis does not forbid marriage of a person who has incapacitating and eventually fatal syphilis if the disease in such a patient is noninfectious

Should both applicants have syphilis, they cannot infect each other, and therefore the disease is not communicable from one to the other The risk in such cases is not to the marriage partner but to their children if there should be any

A candidate who has syphilis in a stage that is or may become communicable but who has not had adequate treatment should ordinarily be required as a minimum to meet the standard required treatment for early and early latent syphilis

If a woman who has syphilis is permitted to marry, the physician must warn such a woman to place herself immediately under medical supervision and usually under treatment for syphilis, preferably with penicillin, if she becomes pregnant.

Some state laws provide that if one candidate for marriage is found to have syphilis, the proposed marital partner must be informed of this fact, after which the certificate may be issued and they may marry.

There are to be considered many factors such as stage and duration of the disease, age and sex of the candidate, amount, kind and method of treatment, so that consultation with a syphilologist may be advised.

Details of operation of the premarital examination laws now in effect in the *United States* illustrate the difficulties which are in many cases imposed on those who cross state lines in order to marry These difficulties arise chiefly from the lack of reciprocity in the acceptance (1) of laboratory reports from out-of-state laboratories and (2) of examination certificates signed by out-of-state physicians

it is performed and a notarized statement of the findings on examination is made, and a copy placed in the hands of the patient. The notarized statement should also be signed by the director of the laboratory performing the serologic test. The patient is informed however, prior to the examination, that such statements may not be acceptable by the state where the nuptials are to be performed.

Treponema pertenue and Yaws. Yaws is known also as pian, frambesia, and perangi.

Treponema pertenue is morphologically indistinguishable from *Treponema pallidum* and, as with *Treponema pallidum*, it is susceptible to trivalent arsenicals and penicillin.

There appears to be no congenital yaws The disease is not transmitted to the fetus through the placenta Mucous patches are uncommon in yaws The disease is not venereal, but is acquired by direct, extragenital contact, more than two thirds of the patients being infected before the age of 15 years. Tabes, paresis, and aortic insufficiency occurring in yaws are often difficult to attribute to yaws.

The disease is transmitted by the organism entering a cut or an abrasion in the skin. The role of flies as vectors has been suggested by Kumm, who found that a fly (*Hippelates pallipes*), widely distributed in the West Indies, fed in large numbers on the open ulcerative lesions, and that *Treponema pertenue* could then be found in the foregut or the stomach, where it remained viable for about 7 hours.

In man one attack of yaws may confer protection against a second attack Immunity develops slowly, thus reinoculation in the first 3 years of the infection may result in a modified attack, but most infected persons are refractory to reinfection after 10 years

There is considerable evidence that yaws confers a measure of protection against syphilitic infection There is some evidence also that syphilis may protect against yaws, or at least modify its clinical course

The primary and secondary cutaneous lesions of yaws are papillomas the tops of which soon become encrusted Necrosis, miliary abscesses and diminution of pigmentation may be observed Tertiary yaws presents no constant features by which the disease can be distinguished from syphilis on histopathologic examination

After examining a large amount of postmortem material Choisser expressed the belief that yaws produces lesions of the heart, liver, adrenal glands, pancreas and testes which are like those produced by syphilis He was able to diagnose the disease only by clinical history The lesions of bone in yaws compare with those of syphilis

Three to 4 weeks after exposure the initial lesion appears. Prior to the appearance of the initial lesion there may be experienced weakness, headaches, pains in the joints and arthralgias These symptoms attended by fever may persist for several weeks.

The primary lesion, the mother yaw, appears on an exposed surface of the body It is a painless and yellow-red papule surrounded by an erythematous zone. The papule increases in size, erodes and ulcerates, the dried exudate forming a dark crust

Six weeks to 3 months later, generalized secondary lesions develop which resemble the primary lesion These secondary lesions are attended by a more severe grade of general symptoms than those present with the mother yaw A localization of a secondary lesion in mucocutaneous junctions of the mouth, nose, or perineum originates a lesion which resembles a syphilitic condyloma Successive exacerbations of more of these same lesions may continue to appear for months to several years

The late sequelae of yaws generally affect the skin and bones. Gummatous nodules and deep, chronic ulcerations or crippling lesions of bones and joints may develop. A destructive ulcerative mutilation of the rhinopharynx (gangosa), a proliferative exostosis of the upper maxilla (goundou), and juxta-articular nodules may occur during the course of yaws

The findings on examination of a patient who has yaws depend on the stage the disease and on any or a combination of the many lesions present, all of whi *resemble those of syphilis.*

DIAGNOSIS. The diagnosis of yaws depends on the appearance of the lesior the history of exposure *in an endemic area, and the demonstration of the organisn* in early lesions either by direct darkfield examination or by contrast visualizatic with India ink or other staining methods

In patients who have yaws a positive response to Wassermann and flocculatic tests develops as regularly as in those who have syphilis.

Treponema carateum and Pinta. The disease pinta is called also mal de l pintos, carate, azul, boussarole or spotted sickness It has been erroneously terme Pinto's disease

Pardo-Castelló and Ferrer stressed the presence of atrophy of the epidermis in la lesions, the absence of pigment in the germinative layer, and the marked excess (pigment in the papillary layer of the corium They were able in all active stages t *demonstrate Treponema carateum in the malpighian layer of the epidermis.*

The incubation period of pinta varies from 5 to 12 months

The symptoms of pinta vary according to the stage of the disease. These stage are (1) the primary stage, (2) the secondary stage and (3) the tertiary stage.

Unlike syphilis and yaws general symptoms are not present in pinta.

On examination the initial lesion or the primary stage is a papule consisting c thickened and degenerated epidermis devoid of the normal amount of skin pigmen The papule is observed to slowly increase in size and in about 2 months it begins t appear reddened and covered with thin scales Smaller but similar lesions appea around the primary lesion These lesions itch At this stage of development th lesions may resemble those of lichen planus.

From 6 to 18 months or longer secondary lesions or pintids appear over bod and limbs These lesions are irregular in size and shape They may be ovoid and 1(*to 15 cm in diameter As time passes larger lesions are formed by the merger o* small ones The surface of the pintid is scaly and the base erythematous an hyperpigmented

The tertiary lesions of pinta are advanced secondary lesions characterized b more profound pigmentary changes. In the skins of lighter color a pink hue may be visible in the areas of depigmentation. Colors of a bluish tint may be observed Black pinta may be present in the skins of the colored races White pinta is observed in the lesions devoid of pigment White pinta represents the mature skin lesion of pinta These mature lesions are attended by atrophy of the skin These mature lesions are commonly present over the exposed extensor surfaces of the hands, arms and over the legs Less commonly do these lesions occur on the face and neck *Cuban pinta is characterized by lesions of the palms of the hands and* soles of the feet

Examination may reveal enlargement of the heart due to valvular lesions of which aortic insufficiency is common The aortic arch may be dilated as with syphilitic aortitis Aneurysms may ensue

Lesions of the central nervous system are uncommon.

Juxta-articular lesions may be present and resemble those of yaws The Charcot type of joint does attend pinta

Enlarged lymph nodes are present throughout the active stages of pinta.

DIAGNOSIS. The diagnosis is based on the appearance of the *cutaneous lesions.* The serologic reactions are not positive during the initial stage; they become positive only during the *early secondary stage in about two thirds of the cases,* and are positive in almost all cases in the late secondary stages

The *disease responds* to treatment with penicillin, arsenicals and bismuth as do yaws and syphilis.

The Borrelias. The borrelias cause a relapsing fever and are transmitted to man by bites of ticks of the genus *Ornithodoros* and the louse, *Pediculus humanus* var. *corporis*, the infection being caused by lice crushed on abraded skin.

***Borrelia recurrentis* and Relapsing Fever** (*Louse-Borne and Tick-Borne*). *Borrelia recurrentis* is a flexible spiral organism which takes the usual bacterial stains It is of widespread distribution. Louse-borne strains have been shown to be infective for argasid ticks, which can then transmit the disease to man; tick-borne strains have been similarly transferred to lice.

Infected ticks (*Ornithodoros turicata, Ornithodoros hermsi, Ornithodoros parkeri* and *Ornithodoros talaje*) have been found in Wyoming, Montana, Idaho, Texas, Oklahoma, Kansas, California, New Mexico, Colorado, Arizona, Utah, and Florida.

Agglutinins and other antibodies may be produced in high titer in the initial attack. However, the serologic activity may change in succeeding attacks The development of mutant strains not susceptible to the antibody previously elaborated may account for the relapse. After recovery from the disease takes place, immunity seems to be present from 3 to 5 years

PATHOLOGY Organisms are particularly numerous in the malpighian bodies of the spleen, which reveals miliary necrotic lesions Hemorrhagic lesions may be found in the gastrointestinal tract and in the kidneys

SYMPTOMS. The symptoms are the same, and are characterized by varying degrees of severity, in the African, Iranian, and American types of the disease. The illness begins with an acute febrile onset 3 to 10 days after inoculation by the louse or tick After 3 to 5 days the fever abates The afebrile period may last 3 to 10 days, and is followed by a second febrile attack during which organisms reappear in the blood, but in a smaller number. Three to 10 such recurring febrile attacks may occur A severe attack of relapsing fever may require weeks or months for convalescence. During convalescence neurologic complications may occur which consist of meningitis Other frequent complications are pneumonia, iritis, parotitis, abortion and retinal hemorrhages.

EXAMINATION On physical examination there are no characteristic findings except the fever During the initial febrile stage there may be large numbers of organisms in the blood, they may be found in the urine in approximately a fourth of the cases. After an average of 4 days the fever declines, coincident with the disappearance of organisms from the blood. As the organisms decrease in number, they become less motile, tend to assume bizarre forms and may agglutinate. During the afebrile period the blood is not infectious for lice

DIAGNOSIS The diagnosis is established by the demonstration of the organism in stained blood films, or by animal inoculation The mortality rate in the endemic infection varies between 2 and 5 per cent, but in epidemics it may be 50 per cent or higher.

***Borrelia vincenti* and Vincent's Angina.** Vincent's angina or infection, an ulcerative stomatitis, is present in association with a coarse, thick, gram-negative rod with tapered ends, the *Fusobacterium plauti-vincenti*, and *Borrelia vincentii*, acting in symbiosis There is no agreement as to whether these 2 organisms are the actual cause of the necrotic lesions, or only secondary invaders Thus Vincent's angina has been ascribed by some to a virus, and by others to a predisposing vitamin deficiency. Vincent's infection may be present in pulmonary disease—pulmonary spirochetosis

The disease is an ulceromembranous stomatitis Other than the presence of the stomatitis there are no characteristic features in Vincent's infection.

The Leptospiras. The leptospiras are characterized by minute elementary spirals running through the body, by the absence of flagella, and by great flexibility of the terminal portion of the organism

***Leptospira icterohaemorrhagiae* and Related Organisms.** *Leptospira icterohaemorrhagiae* is the cause of Weil's disease. *Leptospira grippo-typhosa* is

The findings on examination of a patient who has yaws depend on the stage of the disease and on any or a combination of the many lesions present, all of which resemble those of syphilis.

DIAGNOSIS. The diagnosis of yaws depends on the appearance of the lesions, the history of exposure in an endemic area, and the demonstration of the organisms in early lesions either by direct darkfield examination or by contrast visualization with India ink or other staining methods.

In patients who have yaws a positive response to Wassermann and flocculation tests develops as regularly as in those who have syphilis.

Treponema carateum and Pinta. The disease pinta is called also mal de los pintos, carate, azul, boussarole or spotted sickness. It has been erroneously termed Pinto's disease.

Pardo-Castelló and Ferrer stressed the presence of atrophy of the epidermis in late lesions, the absence of pigment in the germinative layer, and the marked excess of pigment in the papillary layer of the corium They were able in all active stages to demonstrate *Treponema carateum* in the malpighian layer of the epidermis.

The incubation period of pinta varies from 5 to 12 months.

The symptoms of pinta vary according to the stage of the disease. These stages are. (1) the primary stage, (2) the secondary stage and (3) the tertiary stage

Unlike syphilis and yaws general symptoms are not present in pinta.

On examination the initial lesion or the primary stage is a papule consisting of thickened and degenerated epidermis devoid of the normal amount of skin pigment The papule is observed to slowly increase in size and in about 2 months it begins to appear reddened and covered with thin scales Smaller but similar lesions appear around the primary lesion These lesions itch At this stage of development the lesions may resemble those of lichen planus

From 6 to 18 months or longer secondary lesions or pintids appear over body and limbs These lesions are irregular in size and shape They may be ovoid and 10 to 15 cm. in diameter. As time passes larger lesions are formed by the merger of small ones The surface of the pintid is scaly and the base erythematous and hyperpigmented.

The tertiary lesions of pinta are advanced secondary lesions characterized by more profound pigmentary changes In the skins of lighter color a pink hue may be visible in the areas of depigmentation Colors of a bluish tint may be observed Black pinta may be present in the skins of the colored races White pinta is observed in the lesions devoid of pigment White pinta represents the mature skin lesion of pinta. These mature lesions are attended by atrophy of the skin These mature lesions are commonly present over the exposed extensor surfaces of the hands, arms and over the legs. Less commonly do these lesions occur on the face and neck. Cuban pinta is characterized by lesions of the palms of the hands and soles of the feet

Examination may reveal enlargement of the heart due to valvular lesions of which aortic insufficiency is common The aortic arch may be dilated as with syphilitic aortitis. Aneurysms may ensue.

Lesions of the central nervous system are uncommon

Juxta-articular lesions may be present and resemble those of yaws The Charcot type of joint does attend pinta.

Enlarged lymph nodes are present throughout the active stages of pinta

DIAGNOSIS The diagnosis is based on the appearance of the cutaneous *lesions.* The serologic reactions are not positive during the initial stage; they become positive only during the early secondary stage in about two thirds of the cases, and are *positive in almost* all cases in the late secondary stages

The disease responds to treatment with penicillin, arsenicals and bismuth as *do* yaws and syphilis.

blood, their abundant excretion in the urine, and complete development of antibodies in the blood.

Mud Fever or Field Fever. Mud fever or field fever is caused by *Leptospira grippo-typhosa* and is carried by field mice. The infection in these animals is an intense one. Mud fever or field fever is less endemic than Weil's disease, and appears in short epidemics in summer or autumn when there is more chance of exposure to the foul water of swamps. The symptoms are those of a mild form of Weil's disease.

THE BARTONELLACEAE

The genus *Bartonella* of the family Bartonellaceae includes the species *Bartonella bacilliformis* which is infectious to man

Bartonellosis. *Bartonella bacilliformis* is a gram-negative, flagellated organism which stains a distinct red-violet with Wright's or Giemsa's fluid It is very polymorphous, and the maximal morphologic range is seen in the blood of man

The microorganism is transmitted by one or probably several species of *Phlebotomus* or sandfly indigenous to an endemic region It is not transmitted by contact

Bartonellosis is limited to northwestern South America, between latitudes 2 degrees N. and 13 degrees S, at altitudes less than 8,000 feet and more than 2,500 feet Transmission occurs by means of the night-flying and night-feeding *Phlebotomus verrucarum* (see Insects, Chapter 20)

The infection exhibits 2 successive clinical manifestations, of which the second, *verruga,* coincides with, and seems to be an expression of, immunity toward the first form, *Oroya fever* A patient who has had Oroya fever and who then has had verruga and has recovered is immune to further exposures

Oroya Fever (*Carrión's Disease*) The bartonellas in Oroya fever are present within the cytoplasm of cells lining the blood capillaries and the lymph capillaries Infected cells are present in lymph nodes, liver, spleen, bone marrow, kidneys, adrenals, and pancreas, and occasionally in the skin, heart and lungs

Verruga peruana is the nodular cutaneous eruptive stage of Carrión's disease, which differs much from Oroya fever in its clinical manifestations

The incubation period of Oroya fever is from 3 to 15 weeks The symptoms commence with malaise, anorexia and apathy followed by irregular fever and pain The pain is worse at night and disturbs sleep It is situated in the back and extremities. During the period of the fever in the ensuing months there are loss of weight and extreme exhaustion

On examination during the febrile stage of the disease there are extreme paleness and increase of the pulse rate and of the respiration. The superficial lymph nodes are enlarged Usually the liver is palpable, but not the spleen There may be an increase of tendon and superficial reflexes, hemiplegia, facial paralysis, amblyopia, hemianopsia and amaurosis. These are ascribed to vascular lesions of the brain Meningeal findings are common, consisting of meningism, Kernig's sign, headache and persistent vomiting There may be increased pressure of the cerebrospinal fluid and an excess of albumin and of cells in the fluid Frequently bartonellas are not present in the fluid.

The *verruga peruana stage* of Oroya fever is characterized by a nodular cutaneous eruption which usually develops during the period of convalescence. These small warty lesions appear on the face and the extremities, enlarge and become bleeding warty tumors which persist from 1 month to 2 years The eruptive lesions may be small (miliary), of moderate size (nodular), or larger and fungating (mular)

The lesions appear in successive exacerbations They are small (millimeters in size) and nodular, erythematous, and have a smooth, glistening surface. The lesions increase in size, some of them attaining a diameter of 1 cm. The lesions appear sym-

the cause of the disease known in Eastern Europe as mud fever, swamp fever and field fever, and for which field mice seem to be the natural vectors. *Leptospira hebdomadis* in Japan is the causative agent of a disease known as seven-day fever.

Leptospira can penetrate through the intact skin and mucous membranes as well as through these tissues after injury. Usually infection follows contact of the abraded or sodden skin with infected mud or water, but it may follow strangulation by water after one falls into a stream, or the bites of rats, dogs or ferrets. Infection in the United States of America occurs most commonly from contamination of a wound or food with the blood or urine of an infected animal. Mechanical transmission of the infection may occur, as illustrated by the bite of a dog or a ferret that has previously killed a rat Contact with infected dogs or pigs may transmit the disease.

Many human leptospiral infections originate from water or moist objects contaminated with infected urine from rats or dogs.

Weil's Disease. Weil's disease is the commonest form of leptospirosis in the United States of America Human infection occurs from the ingestion of food, and especially of water, contaminated by the urine of infected rats, or from the bite of rats The incubation period is from 6 to 12 days

The progress of the infection is characterized by stages. The first, febrile or septicemic, stage is manifested by chills, fever, headache, generalized muscle aching and pains, anorexia, vomiting, and prostration The fever reaches 102 F (38 9 C) or higher. There may be a lobular type of pneumonia Hemorrhagic herpes may be observed One definitely characteristic manifestation in association with the other symptoms is the presence of a severe conjunctivitis.

During this stage there are spirochetes in the peripheral blood but none in the urine. The leukocyte count varies from 10,000 to 25,000 per cubic millimeter of blood.

On the fifth to the sixth day the temperature recedes to normal limits and then jaundice is in evidence

The second stage of the disease begins on about the fifth or sixth day with the appearance of the jaundice if this occurs By no means do all of those who have Weil's disease have jaundice In those who have jaundice, petechiae, purpura and nosebleed are in evidence. Renal failure may occur in this stage of the disease as the result of a hemorrhagic nephritis In those who manifest failure of renal functional activity with increased concentrations of blood urea and bloody urine a diuresis often initiates the convalescence at about the end of the second week of the disease.

Relapses after recovery occur in many of the cases but are not serious. Meningitis may occur as a complication or independently as a meningitis leptospirosa A most severe leptospiral vegetative endocarditis may follow Weil's disease.

Serious complications of Weil's disease arise in the eyes. They consist of iridocyclitis, optic neuritis and blindness.

The diagnosis during the first 5 to 7 days depends on finding the leptospira in the blood of the patient The most convenient method demonstrating the leptospira is by means of intraperitoneal injection of guinea pigs from which a severe infection ensues; the leptospira can easily be demonstrated in the guinea pigs. In those who do not have jaundice, most commonly the disease goes unobserved by the patient or is not considered as anything that is of a serious nature Specific antibodies begin to appear about the fourteenth day By the end of the third week high agglutinins and lysin titers are demonstrable By the end of the third week the titer is frequently more than 1:10,000. Agglutination in a dilution of 1:300 is considered diagnostic of Weil's disease. This reaction is highly specific The third, or convalescent, stage is characterized by the disappearance of spirochetes from the

Malaria is a disease of the lowlands. It is called also paludism, intermittent fever, chills and fever, Roman fever, Chagres fever, marsh fever, tropical fever, coastal fever and ague. In current use are the English term malaria and the Spanish, paludismo. The malarial parasites of man belong to a class of endoparasites, the Sporozoa, which reproduce by sporulation and have no organs of locomotion. The class includes the following orders: the Gregarinae, the Coccidia, the Hemosporidia, the Sarcospiridia, the Microsporidia, and the Myxosporidia All of these form spores at some stage in their life cycle and are widely distributed in both vertebrates and invertebrates. Of the orders of Sporozoa the Hemosporidia contains the human parasites which are the cause of malaria The malarial parasites belong to the genus *Plasmodium* of the family Plasmodidae.

Four species of *Plasmodium* are parasites of man: *Plasmodium vivax*, the cause of tertian malaria; *Plasmodium malariae*, of quartan malaria; *Plasmodium falciparum*, of estivo-autumnal malaria; and the less known *Plasmodium ovale*, which produces also a tertian form of the disease

The term mixed infection refers to the coincidence of two or more species in the same patient. Mixed infections with *Plasmodium vivax* and *Plasmodium falciparum* are the commonest, next *Plasmodium falciparum* and *Plasmodium malariae*, and least frequent *Plasmodium vivax* and *Plasmodium malariae*. All three species have been reported in the same individual In mixed infections the species appear antagonistic, in patients who have general paresis, inoculated with *Plasmodium vivax* and *Plasmodium falciparum*, one species predominates Masked mixed infections are common In such instances, although only one parasite may be seen in the blood smear, the other may be transmitted by inoculation.

Infection may so arise that one generation of parasites may mature 24 hours before another, resulting in quotidian or daily chills or febrile attacks. Thus a double tertian infection may result with *Plasmodium vivax* and *Plasmodium falciparum* and double or even triple infections with *Plasmodium malariae* The quotidian type of infection may be present in the initial attack, but it tends to return to the tertian or quartan form in recurrent attacks through the decline of the supernumerary group of parasites.

Plasmodium vivax has a world-wide distribution in coastal regions extending from latitude 60 degrees N to latitude 30 degrees S It is the prevailing species in the temperate zones.

Plasmodium malariae is rare in most countries, though it is frequently found in eastern Asia and it has been reported in Mediterranean Europe, southern Asia, Africa, the Philippine Islands, New Guinea, the West Indies, Brazil, Panama and in the southern part of the United States of America

Plasmodium falciparum is commonly limited to subtropical and tropical regions. It is the prevailing species in most tropical countries, and is common in southern Europe. It is present only in the extreme southern portion of the United States of America

The distribution of *Plasmodium ovale* is unknown

The malarial parasites of man are host specific They pass their life cycle in man and an anopheline mosquito The cycle in man is known as schizogony (splitting up of the parasite); that in the mosquito is a phase of sporulation (sporogony).

The bite of an infected mosquito introduces the *sporozoites* into the skin. Eventually the parasites gain access to the erythrocytes. Inside of the erythrocyte the sporozoite develops into a ringlike *trophozoite* and undergoes schizogony Schizogony includes the development of the *schizont* and the division into *merozoites* The enlarging merozoites rupture the cell and are liberated They then penetrate other red blood cells and repeat the cycle. Succeeding generations of merozoites originate trophozoites and become sexually differentiated into *microgametocytes* (male) and *macrogametocytes* (female). This sexual differentiation is in preparation for the sexual cycle in the mosquito.

The morphologic changes of the several species vary, in the peripheral blood, in

metrically on the extensor surfaces of the lower part of the legs, on the forearms, or on the face In some instances the eruption may be present on the trunk, the genitalia, the scalp, the palms or the soles. The eruptions may be localized or general, discrete or confluent. The fully developed lesion remains unchanged in appearance for a long time and then spontaneous regression ensues Pigmented spots may persist for a time after disappearance of the lesions, but scarring does not result.

Bartonella bacilliformis is rarely found in blood before anemia has developed from heavy parasitization and destruction of the erythrocytes. The parasites will be found in normocytes, microcytes, macrocytes, reticulocytes, and normoblasts Disappearance of the visible infection usually coincides with cessation of blood destruction The serum bilirubin is increased, owing to destruction of blood Cultures of blood may be positive after the disappearance of visible parasitemia; visible parasitemia can recur

The diagnosis of Oroya fever requires demonstration of the presence of *Bartonella bacilliformis* in the blood of the patient who has Oroya fever or from the lesion in the verruga stage of the disease. The organism may be found in blood films from a few days after infection until the beginning of convalescence It can be isolated in blood cultures even after the visible infection has disappeared.

The possibility of Oroya fever is considered in a patient who has an acute febrile illness and who, during the 3 months prior to onset of the illness, has been to the regions in South America where the organism of this disease exists.

The mortality rate is more than 50 per cent of those who have severe infection or infection complicated by malaria or other infection. Death occurs in from 10 to 30 days after onset of the illness

STREPTOBACILLUS MONILIFORMIS

Among synonyms for *Streptobacillus moniliformis* are *Streptothrix muris ratti, Haverhillia multiformis, Asterococcus muris, Actinomyces muris ratti* and others

In human beings introduction of the organism into the skin or into the alimentary tract results in invasion of the blood stream with subsequent localization in various parts of the body, and frequently in the joints. In fatal instances ulcerative endocarditis or myocardial abscesses are the causative lesions

There are no characteristic symptoms or even physical signs of infections by *Streptobacillus moniliformis* One syndrome caused by this microorganism is known as Haverhill fever

Haverhill Fever. Haverhill fever begins within a few days after ingestion of infected milk. The onset is with an irregular fever which persists for weeks or months. With the onset of the fever there is a diffused erythematous macular eruption over the extremities, followed by a generalized arthralgia. Often a generalized arthritis ensues.

The diagnosis is made by isolation of the specific organism from the blood. Agglutinins appear in the blood about 10 days after the onset of the infection. Penicillin is a good therapeutic agent.

In all other instances of infection by *Streptobacillus moniliformis* the sickness often follows a rat bite by less than 10 days. There is an irregular and often a relapsing fever. At the beginning of the fever there is often a petechial type of skin eruption, and polyarthritis and leukocytosis are present This syndrome following the bite of a rodent by less than 10 days is highly suggestive.

The diagnosis cannot be made on the basis of clinical symptoms or findings. It is established by demonstration of the organism in cultures of the blood and joint fluid on the special mediums, by mouse inoculation, and by specific agglutination. An agglutinin titer of 1:80 or higher is considered specific for infection with this organism.

engorged with blood and the tubules are obstructed by deposits of hemoglobin and albumin.

The incubation period may be shortened by multiple exposures and lack of resistance, or it may be prolonged; duration of nearly a year has been observed in experimental infections with *Plasmodium vivax*. In the temperate zones tertian infection acquired in the summer or autumn may not cause a chill until the following spring.

SYMPTOMS The symptoms of malaria tend to progress from an acute to a chronic form as the disease progresses The severity and persistence depend on the species and strain of the plasmodium, the resistance of the patient, and the environment. The pernicious type is almost always caused by *Plasmodium falciparum*

The chill often has no recognizable prodromal symptoms When such symptoms are present, they comprise feelings of lassitude, lack of appetite, and deep aching but not severe pains in bones and limbs, and a slight fever. Characteristically each type of malaria is manifested by chills and fever which recur at definite intervals of from 24 to 72 hours.

In tertian malaria (*Plasmodium vivax* and *Plasmodium ovale*) the chills and fever come on alternate days (48 hours). In quartan malaria (*Plasmodium malariae*) the chills and fever occur each third day (72 hours). In malignant tertian malaria (*Plasmodium falciparum*) the chills may come daily or recur on alternate days; the course of this infection is often irregular. In multiple infections fever may recur at irregular intervals; for instance, daily in double tertian infections In low-grade infections and in chronic inadequately treated infections, chills may come at irregularly spaced intervals of days or weeks

In districts where the so-called benign tertian malaria is rampant in the latter part of September and October, at the onset of the malarial season, *the malarial chill is definitely characteristic* The chill usually occurs during the morning hours between 10 A.M and 12 M. The patient, having been active and well during the early morn- [illegible] photophobia. [illegible] rease to sharp [illegible] the hot sunlight increases the intensity of the chill. Soon there is headache, and often severe lumbar backache and deep pains in the thighs ensue. At this period during the chill the temperature reaches its maximum, and perhaps this is one reason for the patient retiring to the shade as soon as the chill commences The chill lasts from 5 minutes to half an hour Toward the end of the chill, sweating begins and lasts from half an hour to an hour and a half After the first few chills the patient often resumes work toward the midafternoon. On returning to work there is a degree of weakness and fatigue The following day there may be no more than a slight amount of weakness. Two days later the chill is often repeated, and so on until adequate treatment is administered, but often the chills cease spontaneously.

In the more severe chills the patient takes to his bed and covers himself with all available quilts or blankets He lies with the knees drawn up to the chest. At first there is shivering which may be superseded by shaking The shaking may be so violent that speaking is difficult or impossible During this stage children often have convulsions

During this stage the face is pale and the nailbeds and lips may be cyanotic. Soon the pale skin becomes flushed and sweating ensues The chill (cold), flushed skin (hot) and the sweating stages all last 4 or more hours

The severity of the chill and fever depends not only on whether it is an initial outbreak or a relapse, but also on the toxicity of the species, the number of parasites in the blood, and particularly, with *Plasmodium vivax*, on the number of generations.

The fever of the tertian and quartan types consists of a series of high elevations of temperature of short duration Temperatures higher than 105 F (40.5 C) are

their effect on the erythrocytes, and in their schizogonic cycle. They differ in incubational periods and in the pathologic reactions of the host. They also vary in ability to develop in different species of anopheline mosquitoes Different specie: show variable reactions to stains

EPIDEMIOLOGY Epidemiologically, malaria is a cosmopolitan disease. It will with any other known disease as a producer of suffering and disability and as a or an indirect cause of death. It is the most important parasitic disease of man be it lowers the health, vitality and physical development of a people; retards intelle social and national progress, reduces economic efficiency, renders useless exte territorial areas and often spreads over such vast areas of lowlands as to mak efforts of public health agencies disappointing.

The conditions that determine the distribution and prevalence of malaria deper the number of human carriers serving as sources of infection, the presence of anopl mosquitoes capable of transmitting the infection, the awareness of the danger mosquito bites, and the economic condition of the susceptible population

IMMUNITY There is some variation in individual susceptibility and resistan malarial infection The susceptibilities and resistances seem to depend somewhat on sex, occupation, and the degree of inherent and acquired immunity. Adults are resistant than children A few persons possess an innate immunity and remain fr the disease even in highly endemic areas. Differences in susceptibility have beer served in Negroes and whites Adult Negroes as well as Negro children from nonma districts show greater resistance than white children.

There is a concomitant immunity which seems to resist a new infection by the type of parasite. There is some residual immunity after the eradication of the par

There is a seasonal variation in the morbidity of malarial infection. For inst *Plasmodium vivax* infections are commoner in the spring and fall and *Plasmo falciparum* infections in the fall These seasonal outbreaks are associated with periodic prevalence of mosquitoes and with clinical relapses

PATHOLOGY The pathologic changes of chronic malaria are characterized by mentation of the cerebral cortex and kidneys, anemia, enlargement and fibrosis of spleen, and enlargement of the liver Capillary thrombosis, hyperemia, hemorrh emboli and pigmentation may be present in many organs which are not other seriously affected The discoloration of tissue is due to the deposition of degrada products of the hemolyzed blood and malarial pigment which occurs free as well a the parasites and phagocytic cells. Malarial pigment is believed to be closely relate hematin, although some investigators claim that it resembles melanin Malarial para commonly cause hemolytic anemia

The *brain* shows increased pigmentation of the capillary endothelium and reg of softening resulting from occlusion of the cerebral capillaries by thrombotic ma of free pigment, pigmented plasmodia (usually the sporulating forms of *Plasmod falciparum*), infected erythrocytes and phagocytes Numerous small hemorrhages produced by the rupture of the distended capillaries In prolonged cases foci of infl mation with proliferation of neuroglia cells, probably of toxic origin, may be pres

In early infections the *spleen* is soft, moderately enlarged, distended with blood, susceptible to rupture In chronic infections the spleen is enlarged, has a firm consiste from hyperplasia of the connective tissues, and is colored slate gray to chocolate pigment in the capillaries and sinusoids Hemorrhagic regions are frequent and schizo are abundant.

The *liver* is moderately enlarged and in chronic malarial infections is firm in text Its color varies from normal to chocolate brown or dark gray Pigment, parasiti erythrocytes, and phagocytic endothelial cells (Kupffer's cells) containing pigments a parasites may be observed. Characteristically there is a focal necrosis with the malar parasites embolic in the capillaries Cloudy swelling, infiltration with fat, and fa degeneration are present.

The *kidneys* are often congested and hemorrhagic owing to the rupture of thro botic capillaries. If death has resulted from the renal involvement, there is an act hemorrhagic glomerulonephritis as the result of embolic blocking of the capillaries the glomerular tufts In chronic disease there may be a secondary contraction of t kidney. The tubular epithelium may be pigmented In blackwater fever the kidneys a

Eosinophils decrease during the febrile attacks and increase in the afebrile intervals, producing a mild eosinophilia during convalescence.

In searching for the malarial parasites of uncomplicated malaria it is well to recall that at the onset of the fever, just prior to the chill and during the course of the chill, the mature schizonts predominate in the peripheral blood in the tertian and quartan types, but are present only in severe infections of the malignant tertian type, in which segmentation takes place almost entirely in the internal organs. At the height of the fever the merozoites predominate in the blood. During the sweating stage most of the parasites have entered the blood cells to complete their development in the subsequent afebrile period.

Diagnosis The presence of malarial parasites in the peripheral blood is diagnostic. If the patient has been under treatment, finding the parasite may not be possible. Repeated examinations of thick films, however, will usually reveal the organisms, especially the resistant gametocytes

The important diagnostic symptom in active infections is an intermittent fever which has been characterized by relapses, in a patient who has had the opportunity to acquire the disease; a fever that does not respond to the administration of quinine or atabrine is not of malarial origin. In latent infections there is a history of relapses following provocative stimulants such as digestive upsets, getting wet and chilled, hot baths, strenuous exercise, purging, alcohol, injections of nonspecific foreign protein, and epinephrine.

Group-specific reactions (precipitins and complement-fixing antibodies) yield vari [illegible]
stan [illegible]

patients are not of diagnostic value for a high percentage of positive reactions are obtained in syphilis, tuberculosis, leptospiroses, leukemia, eclampsia, hepatic diseases, carcinoma, and diseases causing disturbed equilibrium of the serum proteins.

Malaria is a self-limiting disease unless repeated infections occur. *Plasmodium falciparum* infections usually disappear in 1 to 2 years, and *Plasmodium vivax* infections in 4 to 5 years, *Plasmodium malariae* infections persist up to 5 years. Prognosis is favorable in acute *Plasmodium vivax* and *Plasmodium malariae* infections, even without treatment It is grave in *Plasmodium falciparum* infections in which a pernicious type often develops unless adequate early treatment is instituted Chronic malaria in patients who are poorly nourished or weakened by other diseases may terminate fatally.

Complications of Malaria The cerebral type of malaria is serious when caused by any type of infection. Cerebral malaria is manifested by apathy and coma Often there are meningitic or encephalitic delirium, psychic disturbances, paralysis and convulsive seizures Generalized infection may produce hyperpyrexia (temperature of more than 105 F or 40 5 C), headache, delirium, symptoms simulating sunstroke, and hemorrhages in the internal organs. When both the circulatory and nervous systems are involved, the disease may assume the algid form of malaria. In the algid form there is a rapid loss of strength, with cardiac weakness, chilly sensations, perhaps low temperature (97 F, 36 C), and finally collapse and death Dysenteric or choleric symptoms may result from necrosis of the intestinal mucosa but this is usually a terminal event

Blackwater fever occurs most frequently in men and is commonest in tropical countries where malignant tertian malaria is prevalent. Its cause is unknown, but it may be due to an inherent or induced hemolytic tendency associated with hypersensitiveness to, or with inadequate amounts of, quinine. In many instances of blackwater fever the treatment has been inadequate.

Blackwater fever is a frequent complication in malignant tertian malaria During the course of this complication cardiac dilatation, gastroenteritis, hepatitis with

frequent. The tertian fever lasts for 8 to 12 or even 16 hours, the quartan for 10 hours, and the malignant tertian, which has a slower rise and is more prolor for 16 to 18 or even 36 hours. At its climax the febrile curve of *Plasmodium fa arum* infection shows a plateau with minor oscillations that are often mist for an irregular quotidian (daily) infection, and the decline may be interru by one or more sharp peaks. In some cases an irregular fever may persist for we

A latent period of about 3 weeks follows the initial series of intermittent fe attacks and in turn is followed by characteristic relapses, which may recur ov period of years The tendency to relapse is most marked in *Plasmodium mala* infections and least marked in *Plasmodium falciparum*. As the disease progresses latent periods become longer and the relapses fewer.

Relapses are influenced by seasonal changes and climatic variations. Provoca factors that lower resistance, such as exhaustion, diet, alcohol, muscular exert sexual excesses, injuries, exposure to cold, and intercurrent diseases, favor recur attacks Clinically a relapse resembles a primary attack and is difficult to different from reinfection It may be that remissions and relapses are due to the contin presence of small numbers of parasites, the curtailment of asexual development, production of resistant forms, and the retention of the parasites in the tissue c

Plasmodium falciparum frequently causes a pernicious and often fatal form malaria. Malaria of such severity is rarely observed in tertian and quartan infectio

In the natural course of tertian malaria the acute symptoms gradually subs latency develops, and eventually most patients become entirely free of the infecti Infections with *Plasmodium falciparum* either increase in severity or gradually prove, whereas with *Plasmodium vivax* and *Plasmodium malariae* spontaneous missions occur only after frequent relapses.

Chronic tertian malaria, as has been stated, is usually benign, but because reinfections or relapses may become a serious and debilitating disease All degr of clinical manifestations may occur. Persons who do not have clinical sympto may harbor the gametocytes in their blood and so constitute important sources infection Children, who are more susceptible than adults, may show severe sym toms, including fever with or without chills; lethargy and convulsions in the ac stage, and anemia, apathy, debility and splenic enlargement in the chronic stage

In *Plasmodium falciparum* infections, gastrointestinal symptoms consisting nausea, bilious vomiting, diarrhea, abdominal pains and perhaps jaundice may present The abdominal pain may be severe enough to simulate that of an ac biliary obstruction by a gallstone or acute appendicitis or salpingitis When a h fever and bloody dysentery are present the condition may simulate that of an ilei amebic dysentery, bacillary dysentery or acute exacerbation of a chronic ulcerat colitis. Typhoid fever and various rickettsial infections may be simulated by t high fever, headache and delirium.

EXAMINATION. The significant finding on examination of a patient suspected having malaria is the presence of an enlarged spleen The definitely ill malar patient has intermittent fever In the presence of cerebral malaria, signs of encep alitis are present such as apathy, stupor and coma. In some the neck is stiff Vario degrees of heart affections are evidence of cardiac involvement A hemorrha nephritis may be encountered if the kidneys are heavily laden with parasites. In blac water fever the first sign of diagnostic value may be the passage of blood or da urine.

The erythrocytes are reduced in number. They are abnormally resistant to hyp tonic sodium chloride solutions and in severe infections tend to auto-agglomera

Except during febrile attacks the *leukocyte count* is less than normal, the neutr phils are reduced and the lymphocytes and large mononuclears are increased. Th presence of pigment and damaged erythrocytes stimulates chiefly the phagocyt monocytes. During afebrile intervals and convalescence lymphocytes predominat

malarial activity has ceased and the disease has been
and blood smears reveal malarial parasites, the pos
operative infection or embolization is eliminated

Jaundice, anemia, or chills and fever may devel
repeated transfusions of fresh whole blood for an
development may be due to activity from transfuse
infectious hepatitis or hemolytic, Rh or pyrogenic r

FILARIASIS

The filariae of man belong to the genera *Wuchere*
cheilonema, *Mansonella* and *Dracunculus*

Bancroftian Filariasis. The causative organ
known also as *Filaria bancrofti*, *Filaria sanguinis*, an

Wuchereria bancrofti has a world-wide range in
tries from latitude 41 degrees N to 28 degrees S, ext
Australia; in North America it has been observed
at Charleston, South Carolina

Man is the only known definitive host The inter
species of mosquito most commonly associated with
a cosmopolitan night-biting mosquito, and *Aedes vari*
the islands of the Pacific

After penetrating the skin the larvae pass to the
maturity. Reproduction requires the presence of both
filariae migrate from the vicinity of the parent worm t
to the neighboring small blood vessels or are carried i
blood stream

PATHOLOGY Dead and living adult worms are pre
of the lymphatic vessels, lymph nodes and lymphatic
ently cause little injury other than mechanical blockage
microfilariae produce no injury The pathologic chang
adult worms and microfilariae which act as foreign-bo

Obstruction causes edema and lymph stasis, leadin
elephantiasis of various parts of the body Elephantia
fibromyositis or hypertrophy of the hypodermal and
proliferation of collagenous connective tissue The affec
ness, then a hardness, and finally become rough, fis
pyogenic infections

Two opinions are held regarding the relationship o
and elephantiasis (1) These conditions are entirely
worms It is believed by some that lymphangitis an
uncomplicated filarial infections Extensive changes m
eration and absorption of dead filariae (2) They are
chiefly streptococci as secondary invaders Others b
resultant elephantiasis are due to streptococcal inva
persons, and that filarial infections have no direct re
general, statistics reveal that microfilariae may be as
phangitis and elephantiasis as in symptomatic persons
indicate that there is a statistically significant corr

jaundice, albuminuria and nephritis, and rupture of the spleen may occur. The onset of symptoms is sudden, with the passage of dark urine The symptoms may advance rapidly with severe hemoglobinuria, jaundice and rapidly developing anemia. In severe forms of the disease impaired renal function may produce uremia.

Those who have been infected with *Plasmodium vivax* may exhibit clinical signs and symptoms of active malaria within several weeks or months after administration of quinine has been stopped. The *temperature, which is elevated slightly at the* onset, rises gradually or abruptly within a few days to 103 or 104 F (39.4 or 40 C) or it may be completely irregular or of a septic remittent type. Severe shaking chills, which are so characteristic of relapses, may be absent during the first few days of the delayed primary attack despite high fever. Often confusing is the fact that one or two routine smears made early may be negative for malarial parasites. When parasites do appear they may be present in relatively small numbers, in contrast to a relapse

The leukocyte count is usually low, and if the spleen is palpable, one may think of typhoid fever or some other bacterial infection of the blood stream.

In some instances, after suppressive medication has been discontinued, attacks of vivax *malaria may ensue which are manifested by gastrointestinal symptoms.* Nausea, vomiting and abdominal pain and tenderness are common, usually follow the paroxysm, and are rarely of such intensity as to confuse the diagnosis of malaria.

In a small number of cases, however, the abdominal symptoms and signs may precede the paroxysm by a day or two and be of such severity as to suggest a primary acute abdominal condition, particularly acute appendicitis, intestinal obstruction or acute cholecystitis.

Occasionally protracted low-grade malarial activity in some persons who have good immunity may be manifested by slight to moderate anemia, slight icterus, and enlargement of the liver or the spleen or of both Inadequate treatment of frequently occurring mild attacks may also produce the same findings Either there is no fever or, if present, it is low grade Parasites are almost always present in the circulating blood, but their density may be very low

Physicians who have had experience with malarial infections in the tropics have referred to "malaria sensitization and malaria asthma." Urticaria of varying severity may precede or accompany an acute attack of vivax malaria.

It is presumed that these patients have been sensitized by the plasmodia or their products and that, when the former are present in sufficient number to exceed the amount of antibody present, urticaria or some other allergic manifestation follows Urticaria may precede attacks of vivax malaria, and if blood smears are examined, the diagnosis can be made early and time-consuming studies of allergy dispensed with.

Respiratory symptoms in the upper part of the tract, especially during winter months, are common in chronic vivax malaria. Likewise, thoracic pain and rales are not uncommon during an attack These findings in a patient who has a chill and a high fever may suggest pneumonia. Roentgenograms of the thorax do not reveal anything abnormal, and smears will contain parasites, establishing the diagnosis of vivax malaria. In malaria the elevation of temperature is not sustained beyond a few hours after the chill, and the accompanying symptoms, negative roentgenogram, and blood smear positive for parasites should simplify diagnosis if both malaria and pneumonia are considered.

Rupture of the spleen is a most serious and fortunately a rare complication of malaria. The symptoms and signs are so dramatic and the abdominal findings such that the diagnosis is usually made.

Often it has been observed that trauma, general anesthesia or surgical operation may induce a relapse of vivax malaria. Such relapse may occur years after all

infections. The parasite is one cause for the endemic blindness in the Anglo-Egyptian Sudan.

Examination. In the African disease the nodules may appear on the trunk, thighs and arms, and in the Central American disease, on the scalp and head. The number of nodules varies from 1 to 6, however, many may be found.

The disease may involve the skin without the formation of nodules. The tumors are late manifestations of the disease. In the French Sudan the chronic cutaneous manifestations take the form of xeroderma, lichenification, achromia, atrophy and a pseudo-ichthyosis with thick, wrinkled skin. In the American disease there is sometimes a myxedematous-like thickening of the skin over the cheeks and forehead with a bluish pigmentation known as erisipela de la costa.

Ocular involvement frequently is observed when nodules are present on the head. Iridocyclitis with perikeratic injections and a contracted, sometimes irregular, pupil develops. The iris is thickened, altered in color and is sometimes covered with an exudate. It finally becomes adherent by a ring of synechiae to the anterior surface of the lens capsule and undergoes radiate atrophy. A variable punctate keratitis, corneal infiltration with small nests of leukocytes and monocytes, and superficial and deep vascularization of the cornea are present. The microfilariae invade the lymph spaces of the conjunctiva, cornea and iris Involvement of the choroid may spread to the choroidoretinal apparatus, the retinal pigment accumulating in thick plaques. Finally, there are atrophy of the eyeball and entrance of the microfilariae into the sheath of the optic nerve The microfilariae penetrate deep into the choroid and retina from which they have no exit. The eye sets up reactions to the dead microfilariae Individuals hypersensitive to the microfilariae have the severest reactions.

There is often an eosinophilia

Diagnosis Diagnosis is established by finding the adult worms in the nodules and the microfilariae in the skin and nodules In endemic areas the presence of nodules, eosinophilia and ocular lesions is suggestive of onchocerciasis. It is impossible to differentiate the subcutaneous tumors, except by microscopic examination, from dermoid cysts, lipomas, fibromas and juxta-articular nodules

Except in serious ocular involvement prognosis is favorable

Eye Worm (Loasis) (Fugitive or Calabar Swellings). The disease is due to *Loa loa*, also known as *Strongylus loa*, *Filaria oculi humani*, *Filaria lacrymalis*, *Dracunculus loa*, and *Filaria subconjunctivalis*. The worm is indigenous to tropical West Africa

Man is the only definitive host The intermediate hosts are the flies *Chrysops silacea* and *Chrysops dimidiata*, more rarely *Chrysops longicornis* and *Chrysops distincti*, and possibly *Chrysops centurionis* Man is infected by the escape of the infective larvae from the proboscis to the skin when bitten by *Chrysops* The larvae apparently require several years to attain maturity in man

The symptoms do not ordinarily appear until 3 to 4 years after the initial infection The adult worms migrate through the subcutaneous tissues They are particularly troublesome when passing in front of the eyeball or across the bridge of the nose

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nonpitting, subcutaneous swellings are observed on the hands, forearms and in the vicinity of the orbit. They appear spontaneously and disappear in about 3 days There may be present urticarial dermatitis, and soreness from induration of the fascia and connective tissue in the vicinity of the tendon sheaths

Diagnosis is established by recovering the adult worms and more frequently by finding the characteristic microfilariae in the blood during the day The successful surgical removal of the worms effects a cure.

infections in endemic areas when compared with the number who have clinically manifested disease indicates that only a small percentage of infected persons have symptoms.

The symptoms commence with recurring attacks of lymphangitis and fever. There are anorexia, chills, fever, severe headache, malaise and vomiting. The acute attack lasts about 1 week, at the end of which the fever subsides and there is profuse sweating. The attacks often recur periodically, in some persons every few weeks and in others at longer intervals.

EXAMINATION The examination in the early stages of the disease reveals the affected part to be red, painful and swollen, with an erysipeloid that has a sharply defined line of demarcation The lymph nodes are enlarged and tender. After an acute attack the skin and subcutaneous tissues tend to remain swollen

The chronic stage of the disease is characterized by enlarged inguinal lymph nodes, lymphoceles, obstructive lymphatic involvement of the genitalia, and elephantiasis of various parts of the body Elephantiasis commonly affects the lower portion of the legs and the genitalia and may result in extensive deformity. Chyluria is always a suggestive finding though not diagnostic.

On examination in the chronic stage of the disease the elephantiasis is the significant finding The erythrocytes and hemoglobin show no noticeable changes and the leukocyte count may be normal or slightly subnormal. The leukocytes rarely number more than 10,000 per cubic millimeter even during acute attacks of lymphangitis

DIAGNOSIS. Diagnosis in asymptomatic patients is made by finding the microfilariae in the peripheral blood or chylous exudates. Because of nocturnal periodicity the blood in most localities should be taken from 10 P.M to 2 A.M., except where the nonperiodic type prevails.

Clinical diagnosis is based on lymphangitis, lymphatic enlargement, hydrocele, chyluria and elephantiasis Calcified worms may be demonstrated by roentgenologic examination, which is of assistance in locating associated living worms for surgical removal

In asymptomatic infections the prognosis is good, although symptoms may develop later in some patients When severe lymphangitis and elephantiasis are present, the chances of recovery are poor, although afflicted persons may live for years.

Onchocerciasis. The causative organism, *Onchocerca volvulus*, is called also *Filaria volvulus, Microfilaria nuda*, and *Onchocerca caecutiens*.

African onchocerciasis occurs from Sierra Leone to the Congo Basin, and extends eastward across the Congo and the French and British Sudan to Uganda, Nyasaland, and possibly Kenya American onchocerciasis, caused by the same parasite, occurs on the Pacific slope of the volcanic region of Guatemala, centering at Yepocapa In Mexico it is present in the states of Oaxaca, Chiapas and Guerrero. The American form of the disease is largely confined to the mountainous villages of the large coffee plantations.

Man is the only definitive host The intermediate hosts are flies, *Simulium damnosum* and *Simulium neavei* in Africa, and *Simulium ochraceum, Simulium callidum* and *Simulium metallicum in Guatemala and Mexico The microfilariae are* ingested by the fly when it bites the skin Infection of man takes place through contamination of the bite of an infected fly

PATHOLOGY. Onchocerciasis, a chronic infection of the skin and subcutaneous tissues, is characterized by the formation of nodules from 0 5 to 2 5 cm in diameter but occasionally 5 0 cm.

SYMPTOMS. As a rule the patient suffers little discomfort. The nodules may be extremely painful and the affected skin becomes painfully itching

The ocular symptoms, photophobia, iritis and keratitis, occur *some years* after ... hyperemia.

Cutaneous Leishmaniasis. The disease has received various names, according to the locality of its occurrence, among them oriental sore; Delhi ulcer; Aleppo or Natal boil; Bagdad, Lahore or Penjdeh sore; and Biskra button. The causative organism, *Leishmania tropica*, also is known variously as *Helcosoma tropicum*, *Herpetomonas tropica*, *Herpetomonas furunculosa*, *Leishmania furunculosa*, and *Leishmania nilotica*. The life cycle is probably the same as that of *Leishmania donovani*.

Cutaneous leishmaniasis is endemic in the Mediterranean countries of southern Europe and northern Africa, in western and southern Asia, and in central and northeast Africa, and is found in the same countries as kala-azar, but not in the same localities Considered a disease of the Eastern Hemisphere, it has been reported, however, in northern South America and in Central America, although the infecting organism in these regions may have been *Leishmania braziliensis*

The disease is limited to the cutaneous tissues and the mucous membranes. There are atrophy of the epidermis and hypertrophy of the corium Ulceration results from coagulation necrosis and secondary bacterial infection. One attack confers a solid immunity.

The incubation period varies from 1 week to 2 months A small papule appears, continues to enlarge, and acquires a purple color and a glazed surface which give it the appearance of a pustule The lesion becomes covered with brownish scales and by the third or fourth month it has turned to an indurated crusted ulcer, which discharges a thin, offensive pus. Single or multiple sores may develop on the exposed parts of the body. At times the coalescence of ulcers and secondary bacterial infection may result in extensive ulceration and general infection New lesions may be accompanied by chills and fever Uncomplicated sores heal slowly but leave ugly scars.

The presence of the leishmanian parasites establishes the diagnosis. The parasites are found in the exudative material obtained by puncture biopsy from the indurated margin of the ulcer Oriental sore must be distinguished from ulcers due to syphilis, blastomycosis and other infections. The prognosis is favorable.

American Leishmaniasis. This form of leishmaniasis, known as nasopharyngeal or mucocutaneous leishmaniasis, and by many local names, including espundia, uta, forest yaws, bouba braziliana, and pian bois, is caused by *Leishmania braziliensis* (*Leishmania tropica, Leishmania peruviana*).

American leishmaniasis occurs in South and Central America except Chile between latitude 21 degrees N and 25 degrees S , the greatest prevalence being between latitude 5 degrees and 25 degrees S

American leishmaniasis is characterized by ulcerative granulomatous lesions of the mucocutaneous surfaces, particularly the mucous membranes of the nose, mouth and pharynx The lesions are similar to those of cutaneous leishmaniasis The lesions of the mucous membranes of the mouth and nasopharynx take the form of fungating, eroding, indurated ulcers, which may develop into extensive necrotic lesions destroying the

or before, secondary mucomembranous lesions of the mouth, nasopharynx and larynx appear The secondary lesions appear as a thickening of the mucosa which proceeds to formation of nodules and ulceration These lesions are painful and are accompanied by fever, anemia, malaise and, if the larynx is affected, by loss of voice They frequently cause great deformity. The disease may heal spontaneously or result in death from secondary infection and general debility

Examination by physical means is important to assess the general condition of the patient.

The diagnosis of American leishmaniasis is determined by the presence of *Leishmania braziliensis* in stained smears from the indurated edges of the primary or

Trypanosomatidae. The family Trypanosomatidae, of the class Mastigophora and order Protomonadida, includes the hemoflagellates that live in the tissue of their hosts. In the genera *Leishmania* and *Trypanosoma* are species which are pathogenic to man.

Leishmaniasis. Leishmania are of the family Trypanosomatidae of the order Protomonadida of the class Mastigophora

Three species of leishmanian parasites, similar in morphology but differing in geographic distribution, in clinical manifestations and serologic reactions, affect man· (1) *Leishmania donovani* or *Leishmania infantum*, which produces visceral leishmaniasis or kala-azar, (2) *Leishmania tropica*, the cause of cutaneous leishmaniasis or oriental sore, and (3) *Leishmania braziliensis*, the cause of mucocutaneous leishmaniasis or espundia These parasites are flagellate protozoans which occur as small oval or round intracellular organisms chiefly in the reticuloendothelial cells of the skin or the viscera

Leishmanian parasites may be transmitted from one vertebrate to another by contact They pass through a developmental cycle in the arthropod hosts that feed on infected vertebrates Transmission from sandflies, *Phlebotomus papatasii* and *Phlebotomus sergenti*, to a vertebrate host may be by the bite of the insect

***Leishmania donovani* and Kala-Azar or Visceral Leishmaniasis.** This disease, visceral leishmaniasis, also known as Dumdum fever, and febrile tropical splenomegaly, is caused by *Leishmania donovani* or by *Leishmania infantum*. It is endemic in the Mediterranean countries, in Asia Minor, Mesopotamia, southern Russia, India, Turkestan, northern China, the Sudan and Abyssinia. Visceral leishmaniasis occurs in Brazil and Argentina.

The life cycle and transmission of *Leishmania* are not well known Infection has been transferred from dog to dog through infected sandflies. When the infective flagellate gains access to man, it loses its flagellum and assumes the leishmanian form. It multiplies rapidly within endothelial cells, rupturing them, and the freed parasites invade other cells or are phagocytosed

PATHOLOGY At necropsy the liver and spleen are large and congested The bone marrow is soft and red. The lymph nodes are enlarged and there are ulcerations of the colon

SYMPTOMS The symptoms differ in adults from those present in children Both show visceral and sometimes cutaneous manifestations The incubation period in the adult patient is indefinite, and identifiable manifestations do not develop in all infections. The first symptom is often an irregular fever which persists for 2 to 6 weeks, temporarily subsides, and then recurs. Intestinal ulceration may cause diarrhea. Bleeding from the nose and mouth is common.

In infantile kala-azar there are fever, splenomegaly, gastrointestinal disturbances, mental apathy, anemia, emaciation, abdominal distention, cancrum oris, bleeding from nose and gums, and cutaneous hemorrhages

A dermal form of kala-azar characterized by depigmented nodular, granulomatous, nonulcerating lesions of the skin, from which the organisms may be recovered, often appears if there has been insufficient treatment with antimony. The dermal form of the disease without visceral involvement may be an expression of resistance

EXAMINATION. The spleen is enlarged and by the sixth month the liver is increased in size. The lymph nodes are enlarged Anemia, cachexia, leukopenia, edema of the skin and emaciation may be present There is a marked leukopenia. These patients are prone to contract serious septic infections and pneumonia.

DIAGNOSIS The diagnosis depends on finding the parasite in smears or cultures of infected tissues. The infection must be differentiated clinically from enteric fever, malaria and Malta fever

Kala-azar should be suspected in a patient from an endemic area who has chronic irregular fever, leukopenia and splenomegaly.

With proper treatment with antimony the prognosis is good Among untreated patients the prognosis is 90 to 95 per cent fatal

examination of the blood and lymph nodes in the early stages and of the spinal fluid in the late stages.

The prognosis is favorable only if treatment is instituted before involvement of the nervous system occurs. If the patient is untreated, the disease generally proves fatal, although spontaneous recovery may occur in the early stages.

East African Sleeping Sickness. This form of trypanosomiasis is due to *Trypanosoma rhodesiense*, and occurs in Northeastern Rhodesia, South Rhodesia, Nyasaland, Portuguese East Africa and Tanganyika Territory

Irregular, febrile paroxysms, more frequent and severe than in gambian trypanosomiasis, begin after an incubational period of 1 to 2 weeks. There is only slight enlargement of lymph nodes There are edema, weakness, emaciation and myocarditis. Mental disturbances may develop The sleeping sickness syndrome is usually absent and neurologic symptoms are not pronounced

The blood or, better, a lymph node of any person from an endemic area who has symptoms should be examined for trypanosomes. The diagnosis is established by finding the organisms.

American Trypanosomiasis (*Chagas' Disease*) The American form of trypanosomiasis, Chagas' disease, is caused by *Trypanosoma cruzi* (*Schizotrypanum cruzi*, *Trypanosoma escomeli*, and *Trypanosoma triatomae*).

The disease occurs in South America, including Brazil, Venezuela, Chile, Peru and Argentina, and Central America in Guatemala and Panama Cases of the disease in man have not been reported in the United States of America and Mexico, but the trypanosome has been found by several investigators in various species of *Triatoma* in Mexico, California and Arizona

The vertebrate hosts are man, armadillos, bats (Mexico), dogs, cats, monkeys, opossums and wood rats
(a genus of the Reduviid
since the bug frequently
at the junction of cutaneous and mucous surfaces, the injured skin is readily contaminated.

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crithidial and trypanosomal forms The flagellated forms appear in the blood as thin trypanosomes about 20 microns long, or as short, stumpy forms about 15 microns long with pointed posterior ends, and, invading new tissues, continue the reproductive cycle It is possible that the leishmanian forms also invade new cells.

The acute symptoms commence after an incubation period of 1 to 2 weeks. At first there is a high irregular or continuous fever In about 2 weeks there begins to be tumefaction of the face and body due to deposition of mucoid material. Conjunctivitis with edema of the eyelids has been considered to be an early manifestation. The lymph nodes, thyroid, spleen and liver are enlarged on examination

The symptoms of the chronic infection depend on the location of the lesions. Likewise the findings on general examination depend on the lesions present.

The diagnosis is established on finding the parasite. Clinically the disease is differentiated from leishmanian infections, goiter, hypothyroidism, cretinism, chronic malaria and hookworm infection. The examination of blood is usually negative except during fever Laboratory animals may be inoculated with blood or tissues from the patient The complement fixation test with an antigen made from cultured *Trypanosoma cruzi* has proved useful in the diagnosis of chronic infections.

Although spontaneous recovery may occur, prognosis in the acute disease is unfavorable

secondary ulcers. American leishmaniasis must be differentiated clinically from yaws and syphilis. The prognosis is uncertain for untreated patients

Trypanosomiasis. The species of the genus *Trypanosoma* infect both vertebrate and invertebrate hosts.

Three species of trypanosomes are pathogenic to man. *Trypanosoma gambiense* and the closely allied if not identical *Trypanosoma rhodesiense* produce African sleeping sickness, and *Trypanosoma cruzi* produces South American trypanosomiasis or Chagas' disease

The method of transmission is by infective material from open lesions being transferred mechanically by contact or by insects through direct or indirect transmission Direct transmission is accomplished by bites of insects and involves no cyclic development of the trypanosome

Mid-African Sleeping Sickness. This sickness is caused by *Trypanosoma gambiense* (*Trypanosoma ugandense, Trypanosoma hominis, Trypanosoma nigeriense, Castellanella gambiense,* and *Trypanosoma castellani*).

The disease is restricted to the range of its vector, *Glossina palpalis*, in tropical West and Central Africa, limited by Lake Victoria and Lake Tanganyika On the west coast of Africa it is found between Senegal and Angola

PATHOLOGY The most important pathologic changes occur in the lymphatic and nervous systems In the early stages of the disease the postcervical, submaxillary, inguinal and femoral lymph nodes are swollen The spleen and at times the liver are enlarged In the late stages of the disease a chronic leptomeningitis develops The spinal fluid increases in volume. There is a meningo-encephalitis with perivascular cellular infiltration.

SYMPTOMS. The incubational period is usually about 2 weeks, but may be several weeks longer in resistant natives The first symptom of the disease is a fever of a wide diurnal range which lasts for about a week This is followed by a series of febrile attacks followed by afebrile periods. During the afebrile periods the patient feels comparatively well Glandular enlargement, edematous swellings about the eyes and joints, and erythematous skin eruptions are often present The lymph nodes of the postcervical triangle (Winterbottom's sign) are swollen and tender. There may be headache, cramps and a delayed sensation to pain with deep hyperesthesia

After about 12 months the chronic stage begins which is characterized by severe febrile paroxysms and headaches Between the paroxysms there is physical and mental weakness manifested by a morose, indifferent attitude.

EXAMINATION From about 18 months on, a rather profound mental lethargy begins which is the origin of the term sleeping sickness The mental lethargy is progressive. The patient becomes apathetic, dull and drowsy. Speech is not disturbed; conversation is intelligently, but slowly, conducted There is a lack of interest and the voice is weak. At times there may be periods of exaltation followed by deep melancholia. Tremors of the tongue and limbs and even choreiform movements may occur. The gait is slow and shuffling, the patellar reflexes are exaggerated, and there may be a positive Romberg sign, intention tremor and occasionally nystagmus. If the fever is not pronounced or if the patient is examined when afebrile, a disseminated sclerosis may be suspected.

The somnolence increases until finally the patient may fall asleep in the midst of activity. In the terminal stages there is almost continuous sleep. The pulse is rapid, the blood pressure low. The knee jerks are absent and emaciation is extreme. There may be convulsions. Death usually results from a terminal pneumonia

DIAGNOSIS. Trypanosomiasis is suspected when a patient from an endemic area shows an irregular fever, palpable lymph nodes, particularly in the postcervical triangle, erythematous eruptions of the skin, and delayed response to pain with deep-seated hyperesthesia.

Final diagnosis depends on the identification of the trypanosome by laboratory

TOXOPLASMOSIS

The protozoan parasite *Toxoplasma* (a genus of Sporozoa) is pathogenic for a wide variety of mammals and has an extensive geographic distribution.

The life cycle of *Toxoplasma* is incompletely known. Its exact classification is uncertain and the natural mode of transmission is obscure. However, the uneven distribution of latent toxoplasmosis indicates an extrahuman reservoir of infection. Evidence points to insect transmission as a mode of spread from a large potential reservoir of hosts such as dogs, rabbits, squirrels and voles

In experimental toxoplasmosis there is multiplication of the parasites at the site of entry followed by dissemination through the blood stream to every tissue, and invasion of the vessel walls and ultimately of the tissues themselves. The involvement of different tissues depends mainly on their susceptibility, regardless of the portal of entry. The nervous system seems to be especially susceptible

Sabin has made a serologic test which demonstrates the presence of specific serum antibodies By means of this test he has demonstrated that the mothers of some of the affected infants also had or have had toxoplasmosis. In some instances other members of the family also have had the disease. Toxoplasmosis therefore exists in a subclinical or unrecognized form

Among the inmates of institutions for the mentally deficient in the United States a number of previously unrecognized cases of toxoplasmosis have been found. The disease constitutes a known cause of mental retardation and of chorioretinitis.

Performance of the toxoplasmin skin test in Stockholm showed a high percentage of positive reactions The incidence increased from the age of 5 years to the age of 20 years, after which it remained about constant Preliminary investigations of similar kind in northern Sweden showed a far lower percentage of positive results in adults

Necropsy in serologically verified cases of congenital toxoplasmosis reveals an inflammatory process in the organs of the body, but without exception the most pronounced tissue changes are in the central nervous system The infection spreads by the hematogenous route, and the tissue of the central nervous system is especially susceptible The grave character and wide extent of the changes in stillborn infants or infants who died at birth point to fetal transmission of the infection. In all cases the mother's blood gives positive serum reactions with high-titer values Biopsy specimens from the lymph nodes in acquired toxoplasmosis with acute fever and pronounced serologic reactions to *Toxoplasma* show pronounced inflammation, characterized by swelling of the reticular cells and agglomeration of eosinophilic leukocytes and plasma cells in the tissue

Toxoplasmosis occurs in infants, children and adults

It seems that in infants the dissemination of the parasites occurs prior to birth so that in some at birth the original lesions caused by the parasite have largely healed. By the time of birth only the more slowly healing lesions in the central nervous system are left

The general manifestations of toxoplasmosis in children may be first observed when feeding difficulties arise. On examination it may be found that the child has fever, jaundice and enlarged liver and spleen Vomiting and diarrhea are common during the early course of the infection.

There is a predilection for the central nervous system and the eye There is an encephalomyelitis This encephalomyelitis is manifested by first convulsions, muscular twitchings, opisthotonos and hyperactive tendon reflexes Muscular paralysis and weakness of the respiratory muscles and cyanosis may ensue The spinal fluid examination reveals a pleocytosis, xanthochromia and increased concentration of protein

Ocular manifestations are common and result from direct involvement of the intrinsic structures of the eye and secondarily from involvement of the cranial portion of the central nervous system. The intrinsic manifestations consist of iridocyclitis with synechiae, cataract secondary to uveitis, vitreous opacities and fibrosis

Histoplasma capsulatum and *Blastomyces dermatitidis* In the doses commonly used for skin tests, individuals who have positive reactions to coccidioidin will give cross reactions with histoplasmin or blastomycin There seems to be a larger amount of this hypothetic common antigen in *Blastomyces dermatitidis* and *Histoplasma capsulatum* than in *Coccidioides immitis* Therefore histoplasmin, blastomycin and coccidioidin should be used simultaneously to determine which gives the greatest reaction.

In subclinical coccidioidomycosis and in many instances of blastomycosis, the infection does not stimulate the production of complement-fixing antibodies in detectable amounts However, in the progressive form of these three mycoses, complement-fixing antibodies are present regularly and persist even when the patient becomes anergic and the skin test is negative

Cross complement fixation does not occur between coccidioidomycosis and histoplasmosis. Those who fix complement in a high titer with histoplasmin also fix complement, but to a lower titer, with blastomycin This necessitates simultaneous tests with blastomycin and histoplasmin Some patients with histoplasmosis have a higher complement-fixing titer for blastomycin than other patients who have a true blastomycotic infection

The Actinomycetales. The Actinomycetales are an order under the class Schizomycetes. There are three families, Mycobacteriaceae, Actinomycetaceae and Streptomycetaceae in the order Actinomycetales The Actinomycetaceae contain two genera pathogenic to man, *Actinomyces* and *Nocardia*

The Actinomycetes and Actinomycosis. The actinomycetes, growing in the form of a branched mycelium, have characteristics intermediate between those of bacteria and molds Actinomycetes isolated from animals and man show wide variations in structure The parasitic actinomycetes may therefore be grouped provisionally in a single species, *Actinomyces bovis*, which causes actinomycosis

Actinomycosis is a subacute or chronic, progressive disease characterized by the development of indurated, granulating, connective tissue swellings, limited suppuration and pus which often resemble tuberculous manifestations

The pathologic changes in actinomycosis are necrosis, granulation tissue and the formation of dense fibrous tissue Sulfur granules are characteristic

Material obtained at necropsy after death due to infection with Actinomycetaceae reveals varying degrees of pathologic processes, some caused by the mycotic organisms, and others by secondary bacterial invaders For example, Weed and Baggenstoss recorded the bacteriologic findings in 35 cases in which diagnosis of actinomycosis was established by postmortem observations.

The organism *Actinomyces bovis* could be demonstrated in histologic sections with reasonable certainty in only 21 instances, with considerable doubt in 3 and not at all in 11 In 2 of the 11 instances there were different gross and microscopic features, and the observations were suggestive of nocardiosis *Nocardia* was isolated in pure culture from 1 of these In 13 of the 21 in which *Actinomyces bovis* was present, it was possible to demonstrate microscopic evidence of mixed infection The probable clinical significance of the organisms associated with *Actinomyces bovis* was reflected in the presence of renal involvement in 12 of 16 (pyelonephritis and formation of abscess) and nonactinomycotic brain abscesses in 5 Evidence from the study of fixed tissues indicated considerable variation in the detailed structure of colonies presumed to be *Actinomyces bovis* The variations included presence or absence of clubs, apparent fusion of clubs, staining reaction of clubs by the Brown-Gram technic, number of filaments, length of filaments, some of them being very short and closely resembling diphtheroids, and compactness of the colonies, some of which showed almost diffuse growth The sections also showed considerable variations in the amount of fibrosis. The presence of sulfur granules and the microscopic observations, usually considered characteristic of actinomycosis, may be produced by organisms other than *Actinomyces bovis*. In many instances cultures are necessary to establish the differentiation.

It may be possible to differentiate between the pathologic process produced by the

tuberculosis, which more commonly involve the same structures as do the mycoses, making the diagnosis of generalized mycotic diseases at times difficult and often entirely unsuspected until the offending organism is found by smear or culture.

The mycoses may be of either endogenous or exogenous origin.

The mycoses of endogenous origin are distributed uniformly. Men of all races are infected more frequently than women, and adults are infected more frequently than children.

In contrast with the mycoses of endogenous origin, those of exogenous origin are more numerous The exogenous mycoses, such as sporotrichosis, nocardiosis, aspergillosis, penicilliosis and mucormycosis, are uniformly distributed, whereas coccidioidomycosis is found in California, Arizona, New Mexico, southern Utah and the southwestern part of Texas *Histoplasma capsulatum* is widely distributed, but it seems to prefer to live in the Mississippi valley, the Ohio River valley and the Appalachian area Blastomycosis is a disease which is more frequent in the Mississippi valley and in the southeastern states than elsewhere Chromoblastomycosis, mycetoma and rhinosporidiosis occasionally are observed in the southern part of the United States

The exogenous types of fungous infection are commoner and more severe in Negroes, Mexicans and Filipinos than in light-skinned peoples. In these dark-skinned peoples coccidioidal granuloma is a highly fatal disease

Generally a mycotic infection is suspected in every patient who has chronic draining sinuses, whose sputum is negative for tubercle bacilli, and from whom has been obtained a negative biopsy study for neoplasia and a Papanicolaou smear negative for malignant cells The presence of *Cryptococcus neoformans* (*Cryptococcus histolyticus, Torula histolytica*), *Coccidioides immitis, Histoplasma capsulatum, Blastomyces dermatitidis, Sporotrichum schenckii, Actinomyces bovis, Nocardia asteroides, Rhinosporidium seeberi* or the various organisms which cause chromoblastomycosis or maduromycosis in the sputum or other discharges establishes a diagnosis. The presence of *Candida albicans* (*Monilia albicans*) or one of the various species of *Geotrichum, Aspergillus, Penicillium* or *Mucor* does not necessarily imply that these organisms are producing disease These fungi are often proved to be accidental or secondary invaders rather than the primary etiologic agents The presence of *Actinomyces bovis* in the gums or about carious teeth, in saliva, or in sputum which contains a considerable admixture of saliva, without a definite demonstrable focus in the mouth, also is considered an accidental finding even though pulmonary disease is present

The experienced mycologist can make a good many correct diagnoses by a direct study of the sputum or of the pus from discharging sinuses He examines the material unstained, with or without the addition of a few drops of 10 per cent solution of sodium hydroxide, and with or without staining suspected granules by Gram's method. In some instances the use of the methods usually employed for the demonstration of tubercle bacilli, provided the decolorization with acid alcohol is not excessive, is diagnostically helpful

Skin tests are of definite but limited value in the diagnosis of mycotic infections. Clinical and subclinical infections with *Coccidioides immitis* and *Histoplasma capsulatum* regularly induce a tuberculin-like sensitivity to coccidioidin and histoplasmin, respectively. Hence a negative result of a skin test eliminates the possibility of these mycoses unless the patient has an anergy as the result of a progressive terminal infection. Infections with *Blastomyces dermatitidis* may or may not induce sensitivity; therefore a negative result of a skin test to blastomycin cannot be used to eliminate the possibility of this disease Hypersensitivity to autogenous vaccines has been observed in most of the other mycoses, but there are insufficient data to enable evaluation of their frequency and significance.

It seems there is a small amount of an antigen common to *Coccidioides immitis*,

the skin, projection of the lesion beyond the surrounding integument, multiple nodules, with the formation of ridges and furrows in the creases of the skin of the neck and the presence of multiple scars are strongly suggestive of *Actinomyces bovis.*

Actinomycosis must be differentiated from tuberculous lesions. A tuberculoma opens as a single sinus and is painless, without the boardlike hardness of actinomycosis Tuberculous adenitis is a condition seen in early life, while actinomycosis may occur at any age. The biopsy may reveal epithelioid cells and giant cells, typical of the tuberculoid structure, but no granules will be found Periosteal sarcoma, Hodgkin's disease, lymphosarcoma and branchial cyst are distinguished by surgical removal and histologic study.

Metastasis from a cutaneous epithelioma appearing in the submaxillary region may simulate actinomycosis.

Thoracic Actinomycosis. The thoracic viscera may be affected by spread of a cervicofacial infection through the fascial planes of the neck. Actinomycotic lesions tend to spread widely by contiguity, sometimes pointing toward the skin and forming fistulas that tend to heal and re-form elsewhere. The organism may be disseminated through the blood, or, in the lungs, through the bronchi Bone is seldom affected interstitially except in the jaws.

If there is not present an actinomycotic infection of the head and neck, the manifestations of thoracic infection are not materially different from those of tuberculosis. The diagnosis has to be made by identification of the offending organism. (See Diseases of Respiration, Chapter 9)

Abdominal Actinomycosis. Actinomyces bovis exists as a saprophyte in the mouth, respiratory tract and gastrointestinal tract of man and animals. It becomes pathogenic only if it penetrates a break in the mucous membrane produced by trauma or disease. This uncommon disease occurs most frequently in men in the second to fifth decades. It has a wide geographic distribution and affects persons in all occupations Many cases of abdominal actinomycosis follow acute perforative or ulcerative disease of the gastrointestinal tract, very often rupture of the appendix The organism spreads by direct extension through adjacent tissue and tends to form fistulous tracts through the abdominal wall.

In still rarer instances of abdominal infections the first evidence of the disease is an abdominal mass, and the true nature of the process is discovered by histologic and bacteriologic study of materials removed surgically or later from fistulous formation postoperatively

Apparently primary infection of the stomach with *Actinomyces bovis* has been recorded

The diagnosis of abdominal actinomycosis cannot be made without demonstration of the organism by direct examination or culturally. Sulfur granules may be present in some instances. In other instances the organisms may be like *Actinomyces bovis* but no clubs accompany the granules. Sulfur granules, if present, are of diagnostic value If they are not present, the diagnosis rests on demonstration and identification of the organism by other means

The Nocardias (Saprophytic Actinomycetes) and Nocardiosis. Pathogenic aerobic acid-fast and nonacid-fast actinomycetes are free-living plant organisms which cause disease by air-borne contamination or by introduction into tissues through trauma Species of *Nocardia* are found in lesions of man and animals, and, unlike *Actinomyces,* are free living in nature as contaminants on the skin and as inhabitants of soil and in plant disease

The genus *Nocardia* includes several different species: (1) *Nocardia asteroides,* (2) *Nocardia brasiliensis,* (3) *Nocardia madurae,* (4) *Nocardia pelletieri* and (5) *Nocardia paraguayensis* (Names of species are those preferred by Conant, page 582, *Bacterial and Mycotic Infections,* edited by Dubos)

aerobic *Nocardia* and the anaerobic *Actinomyces bovis.* When it is possible, such differentiation is made, and is helpful diagnostically and therapeutically.

In reports from the pathologists it is well to know that not all species of pathogenic actinomycetes produce club-bearing granules, and clinically granules are not in evidence in all cases of actinomycosis Other infections produce granules as well. Granules with clubs are formed under certain conditions by such organisms as *Coccidioides immitis* and strains of *Aspergillus, Sporotrichum* and *Monilia.*

There is no evidence that actinomycosis is communicable. *Actinomyces bovis* is a true parasite of mucous membranes, never found in nature apart from a parasitic or pathogenic habitat, it occurs on mucous membranes, possibly in the absence of any disturbance, certainly in the presence of low-grade nonspecific inflammatory processes, for example, of the gums. It produces disease as an endogenous infection

The lesions of actinomycosis are subacute or chronic and they tend to appear on the skin (in primary cutaneous actinomycosis) or in one of three sections of the body: (1) head and neck, (2) thorax and (3) abdomen. However, the disease is often widely disseminated through the blood and then many organs may be involved including bones other than the jaw.

Primary Cutaneous Actinomycosis The term primary cutaneous actinomycosis designates the form of the disease in which the infection does not spread from a neighboring mucous membrane or arise from a systemic infection. All species of actinomycetes have been suggested as etiologic agents in primary actinomycosis

Actinomycosis of the Head and Neck. The commonest site of actinomycosis in both man and animals is the mouth and neighboring passages.

Cervicofacial actinomycosis apparently originates from the mouth, but affects the soft tissues and skin of face and neck, the tongue and, secondarily, the maxillary bones. The salivary glands, larynx, thyroid and lacrimal glands, the orbit and even the brain may be involved The lesions most commonly appear on the cheek or submaxillary skin, and are characterized by indurated or edematous swellings, bluish or reddish, with a tendency to form a series of irregular folds separated by furrows, the healing lesions forming scars as new lesions develop.

The jaw, when affected, becomes swollen. The tissues are at first hard and indurated, simulating a malignant tumor Later, necrosis takes place inside the tumor and draining sinuses form.

On the tongue the infection is manifested by indolent ulcers and formation of sinuses.

The onset of the disease is insidious The usual history is of chronic periodontitis surrounding a carious tooth or teeth, often going back for several years. In most cases the acute stage of actinomycosis is preceded by the removal of infected teeth. Twenty-four to 48 hours after extraction of such a tooth, there is a slight rise of temperature, with edema and swelling of the soft tissues about the mandible There are alternate regression of the active process and recurrence with exacerbation Each recurrence is accompanied by fever (temperature up to 101 to 102 F or 38 3 to 38.8 C) and reduces the resistance of the tissues to the parasite. There may be hoarseness and dysphagia

On examination the lesion consists of firm, subcutaneous, purplish tumors which may have gradually softened, ulcerated and broken down, leaving fistulous tracts In the acute form of the disease all the soft tissues as far down as the clavicle may show solid dense edema, with bluish red erythema. There is usually central necrosis in the region in which the infection originated, with little pus but with suppuration of a clear, straw-colored fluid As sinuses form, secondary bacterial invasion, particularly that of staphylococci and streptococci, is present.

The diagnosis of actinomycosis of the face and neck depends on the presence of both macroscopic and microscopic granules of actinomycetes in the pus and the demonstration of the organisms by cultural means. The dark red discoloration of

The cutaneous involvement may be primary or appear as a manifestation of an already established systemic infection. The lesions appear as acneform pustules, punched-out granulomatous ulcers, subcutaneous tumors or deep-seated abscesses. A cutaneous infection may progress to generalized infection with involvement of the brain, meninges, lungs, liver, spleen, pancreas, thyroid and aorta The primary pulmonary infections resemble neoplasm or tuberculosis. The primary brain infection may resemble an encephalitis, acute or chronic meningitis such as a tuberculous meningitis, or may resemble brain tumor, brain abscess, or degeneration or syphilis of the central nervous system

Sputum, pus, gelatinous exudates or sediment of centrifuged spinal fluid contains the fungus. In pulmonary infections the organism may be revealed in the sputum or exudates The pathogenicity of the fungus is revealed by its effect on mice.

Blastomyces dermatitidis and North American Blastomycosis (*Gilchrist's Disease*). *Blastomyces dermatitidis* is a spherical, thick-walled, budding, yeastlike fungus It produces a granulomatous infection of the skin and internal organs very similar clinically and histologically to tuberculosis

The cutaneous infection commences as a papulopustule which spreads peripherally, showing a granulating base covered with a bloody exudate and a raised papilliform or verrucous border with miliary abscesses. Spontaneous healing of the centers of such lesions produces characteristic thin scars surrounded by a raised and spreading border. The papulopustules are situated on the face and neck, on the dorsa of hands, wrists and forearms, ankles and legs, and in the perineal regions. By direct extension or hematogenous spread the lesions appear anywhere on the body as multiple, subcutaneous, gumma-like processes which rupture spontaneously, freeing bloody pus

In systemic blastomycosis the lungs are most frequently infected and show the most extensive lesions In the presence of septicemia, however, subcutaneous tissues and bones, the vertebrae and ribs, are commonly affected The central nervous system and the liver, spleen and kidneys may be involved.

The diagnosis is based on demonstration of the *Blastomyces dermatitidis* in the pus from miliary abscesses at the border of cutaneous lesions or from subcutaneous lesions of sputum Spinal fluid and urine should be centrifuged and the sediment examined In all of these materials *Blastomyces dermatitidis* should be identified by culture before a diagnosis is made

Blastomyces brasiliensis. This fungus is large, thick-walled, single budding or multiple budding, and yeastlike. It produces a granulomatous infection of the mucous membranes of the mouth, lymph nodes and internal organs which is known as South American blastomycosis, paracoccidioidal granuloma, Lutz-Splendore-Almeida disease, and Almeida's disease

Pus and scrapings from the buccal mucosa and the skin lesions, pus from fluctuant nodes, and smears of biopsied nodes should be examined as fresh preparations and cultured for diagnosis

Rhinosporidium seeberi. The infection rhinosporidiosis is attributed to *Rhinosporidium seeberi* (called also *Rhinosporidium kinealyi*). Natural infections have been observed in horses, mules and cows The disease occurs most frequently in children and in young adults but it may appear at any age. Persons who frequently swim and dive in stagnant fresh water are especially liable to this infection.

Itching in the nose and a mucoid discharge are the first symptoms. Subsequently a granuloma develops on the nasal mucosa and this may eventually become a pedunculated polyp which is pink or purplish Occasionally the granuloma develops in the larynx, on the conjunctiva, in the ear, on the penis, in the vagina or in the rectum Papillomatous lesions may develop on the skin of the face.

The presence of a nasal polyp suggests the diagnosis. It is easily confirmed by direct examination and demonstration of the large sporangia

Nocardia asteroides is the only species which shows pathogenic tendencies and even this species varies greatly in its ability to produce infection. *Nocardia asteroides* infections are not common. They do not occur spontaneously in any animal except man. In the large majority of cases the diagnosis is made at the time of necropsy. In those instances in which the diagnosis is made during life, the organism is demonstrated late in the course of the disease.

Nocardiosis Nocardiosis is a chronic suppurative infection of the superficial tissues and the bones or a generalized infection usually originating in the lungs

Nocardiosis involving the subcutaneous tissues and bones (mycetoma or maduromycosis) is characterized by multiple tumefactions and draining sinuses from which "granules" (yellowish white, red or black) are expressed in the pus or found in the tissues

In a nocardemia the organisms may be filamentous, bacillary or coccoid. They are acid-fast, and may be present in the sputum, spinal fluid, or pus from subcutaneous abscesses

Maduromycosis of the lower extremity is termed Madura foot. The characteristic lesion with pain, swelling, and formation of sinuses, and eventual clubbing and marked deformity of the infected member, develops only after months or years. Infection spreads by extension through adjacent tissues, with destruction of bone, multiple abscesses with rupture, and with no systemic reaction unless secondary bacterial invasion is established The walls of sinuses and abscesses may show only a chronic inflammatory reaction. Further development of the acute purulent abscess results in a surrounding layer of granulation tissue

Pulmon[illegible]
with sputum [illegible]
may reveal [illegible]
in the body may be affected as the result of a nocardemia

The generalized form of the disease is caused by *Nocardia asteroides*. When there is a nocardemia, the brain commonly is involved. When the infection once is established in the brain, there are symptoms of either brain tumor or brain abscess. In some the symptoms may be those of a meningitis resembling that of tuberculous origin with minimal or no findings in the lungs

Generalized nocardiosis may be manifested very much as is tuberculous infection of the lungs and pleura with hematogenous spread throughout the body, especially to the brain and meninges

The diagnosis of nocardiosis is established by the demonstration, by culture, of the nature of the offending organism Pus from the draining sinuses, scrapings from the walls of sinuses and biopsy sections should be examined for actinomycotic granules.

The Fungi Imperfecti. The Fungi imperfecti contain practically all of the fungi pathogenic to man other than *Actinomyces* and nocardias

The Fungi imperfecti are identified by the mycologist by their structure: *macro-* [illegible]

[illegible]a,
namely, *Microsporum*, *Trichophyton* and *Epidermophyton*. These were considered in Chapter 8.

Cryptococcus neoformans (Torula). *Cryptococcus neoformans* is a yeastlike, nonsporulating, nonmycelial, budding fungus characterized by the development of a wide capsule. It may involve the skin but it has a marked predilection for the central nervous system and produces a subacute or chronic infection of the meninges (Torula meningitis) or lesions simulating brain tumor or brain abscess The infection is known generally as cryptococcosis, torulosis, European blastomycosis, and Busse-Buschke disease.

Thirty-eight per cent of Ohio children who reacted neither to histoplasmin nor to tuberculin showed pulmonary calcifications Perhaps the recent development of a complement fixation test for histoplasmosis will aid in more accurate diagnosis of that infection. If specific, such a test might be of great value in the differential diagnosis of early precalcific pulmonary infiltrates

The symptoms of histoplasmosis are varied Since the disease is reticuloendothelial cytomycosis the symptoms are dispersed in the order of the reticuloendothelial system. Generally the symptoms are those of a systemic febrile illness often with the pulmonary symptoms being more manifest than other symptoms.

On examination during the acute phase of the infection often there is present a systemic febrile disease with enlargement of the liver and the spleen In other instances lymph-node enlargement may predominate, and the findings resemble those present in Hodgkin's disease, leukemia, lymphosarcoma or aplastic anemia In still another group pulmonary changes may predominate, and infection may be complicated by, or superimposed on, pulmonary or general tuberculosis

The parasites appear in the cells of the reticuloendothelial system They may be found in thin smears of peripheral blood or in sections of the lymph nodes, spleen, or material obtained by sternal aspiration. Anemia and leukopenia are present.

In the quiescent stage or the healed stage of histoplasmosis diffusely scattered pulmonary lesions are characteristic. Postulating that these pulmonary calcifications might represent a primary, benign form of histoplasmosis, workers have attempted to discover early pulmonary infiltrates in the endemic areas which could be attributed to histoplasma infection Studies in school children of Kansas City disclosed patients who when originally seen gave roentgenograms of the chest which were interpreted as normal and negative histoplasmin reactions and in whom there subsequently developed pulmonary infiltrates or hilar adenopathy or both, along with a positive reaction to histoplasmin These infiltrations could not be distinguished roentgenographically from active pulmonary tuberculosis The *Histoplasma capsulatum* was isolated from one of the children who had precalcific lesions.

The development of calcification in some of these precalcific lesions has been observed, so that the pathogenetic process has been followed from the negative roentgenogram of the chest and negative histoplasmin reaction through the appearance of the parenchymal infiltrate (with concurrent change in cutaneous sensitivity) to the final calcified focus in the lung associated with a positive reaction to the histoplasmin test

Negative reactions to tuberculin tests in the presence of pulmonary calcifications were formerly interpreted as being due to a loss of tuberculin allergy. However, it has been shown that there is an exceptionally high incidence of pulmonary calcifications among residents in the Ohio and Mississippi valleys and that the incidence of tuberculin negativity in these people is too high to be explained on grounds of anergy

As with coccidioidin, the histoplasmin skin test is performed by intradermal injection of 0 1 cc of diluted histoplasmin on the arm A dilution of 1:1,000 is usually employed, although stronger dilutions (1 100) are also used. The chief value of the histoplasmin test lies in its use in the differential diagnosis of unexplained pulmonary infiltrates or calcifications, especially in tuberculin-negative reactors. In the patient who has acute, disseminated histoplasmosis, analogous to the anergy of those with disseminated tuberculosis or coccidioidomycosis, reaction to the skin test is often negative.

Coccidioides immitis and Coccidioidomycosis. *Coccidioides immitis*, the cause of coccidioidomycosis, is a pathogenic fungus of the family Endomycetales. It is a spherical, thick-walled, endospore-filled organism that seems to be highly infectious to different animals and to man The fungus has been isolated from rodents, dogs, sheep and, in some districts, from cattle.

In the United States *Coccidioides immitis* seems to thrive in certain endemic

The disease runs a chronic course but it is not of itself fatal unless it causes obstruction of the larynx or the esophagus.

Candida albicans. *Candida* (formerly called *Monilia*) is a genus of yeastlike fungi which may produce mycelia but not ascospores. These organisms, particularly *Candida albicans*, are equivocal disease producers. The commonest form of moniliasis is thrush, a disease characterized by the formation of gray-white patches on the buccal mucous membranes, tongue and pharynx of feeble patients. In babies the disease may have been acquired during birth from a mother who had a vaginal infection.

Candida albicans, the causative organism of moniliasis, is an oval, budding, yeastlike fungus producing both blastospores and pseudomycelium in tissue and exudates. It is frequently found in the normal mouth and intestinal tract or as a secondary contaminant in recognized diseases. Its exact etiologic significance in any disease process is difficult to establish

Candida albicans, in addition to the production of infections of the mucous membranes of the mouth (thrush) may cause vaginitis or vulvovaginitis; irritations of the intertriginous areas and interdigital webs of the hands and feet, infections of the nails (onychia and paronychia); and systemic infections such as bronchopulmonary, or generalized infection of lungs, lymph nodes, liver, spleen and meninges

Vulvovaginitis, caused by infection of the vaginal mucosa and vulva, is a thrush-like infection characterized by irritation, pruritus and a thin discharge

Lesions on the hands follow maceration of tissue by continued immersion in water and therefore afflict housewives, waiters, chefs and bartenders.

Infection of the nails (onychia and paronychia) is characterized by swelling at the nail bed which may be painful and resemble a pyogenic infection, and by thickened, transversely grooved nails.

In the lungs *Candida albicans* may cause a mild bronchopulmonary moniliasis with persistent cough, or a more extensive pulmonary moniliasis resembling miliary tuberculosis with cough, fever, dyspnea, thoracic pain, hemoptysis and night sweats accompanied by signs of pleural thickening and consolidation.

Moniliids (candidids) occasionally accompany localized infections. Such lesions are sterile and appear on the body as a result of sensitivity to the yeastlike fungi found in lesions elsewhere in the body

Histoplasma capsulatum. Histoplasmosis is caused by *Histoplasma capsulatum*, a species of Fungi imperfecti.

The site of entry is uncertain; the skin has been suggested with possible bites or infestations by parasites as the mode of entry, but the portal most commonly accepted is the lungs They appear to be the site of the oldest and densest involvement.

Histoplasmosis occurs in temperate and subtropical climates and particularly in the Ohio and Mississippi valleys in the United States of America.

Pathologic alterations consist of an enlarged spleen and gray or white nodules in the lungs, liver, spleen, the intestine and the pulmonary and peritoneal surfaces Pathologically the disease is a reticuloendothelial cytomycosis Henderson, Pinkerton and Moore reported a case of histoplasmosis in which the chief lesion was an ulcerative enteritis. Examination of stools in such cases may reveal the histoplasmas The almost constant involvement of the mesenteric lymph nodes points, according to Henderson, to the gastrointestinal tract as the portal of entry

Residual lesions, nodular foci as well as cavities in the lungs, have been described in histoplasmosis. A characteristic feature is the occurrence of disseminated infiltrates resulting in "snowstorm" calcifications. If *Histoplasma* is the causative agent of snowstorm calcification, this presupposes the presence of the fungus in soil, an assumption which has been verified by Emmons. He also has pointed out the cross sensitivity between histoplasmin and blastomycin. The endemic areas of blastomycosis and histoplasmosis overlap. Tissue forms of blastomyces may resemble histoplasma forms.

the body, for example, in the lungs, larnyx, lymph nodes, bones, joints and central nervous system.

DIAGNOSIS OF COCCIDIOIDOMYCOSIS. The diagnosis of coccidioidomycosis in all forms is determined by the presence of *Coccidioides immitis* in pus, sputum, gastric contents, pleural fluid and spinal fluid

Complement-fixing antibodies and precipitins can be demonstrated in the serum of patients infected with *Coccidioides immitis.* The complement-fixing antibodies have the same significance as in blastomycosis; that is, they indicate spreading infection and poor prognosis. Hypersensitivity to the fungus can be demonstrated by the coccidioidin skin test. Positive results of the test usually develop in 3 to 21 days after infection, and a delayed tuberculin-like reaction occurs in 24 to 48 hours.

In the presence of a positive reaction to both the tuberculin and the coccidioidin skin test the diagnosis is difficult unless tubercle bacilli can be demonstrated. In the absence of tubercle bacilli a presumptive diagnosis of coccidioidomycosis can be made if there is a history of possible exposure in an endemic area; if there is roentgenologic evidence of a pulmonary lesion, usually a solitary cavity or nodular density, which reveals no change after months or years of observation, and if there is positive reaction to the coccidioidin skin test The diagnosis of coccidioidomycosis in the presence of active pulmonary tuberculosis as revealed by sputum containing tubercle bacilli cannot be made

An important feature in pulmonary coccidioidomycosis is the well-being of the patients, often without symptoms, unless there are pulmonary hemorrhages from a cavity. The presence of a coccidioidal cavity in a lung in the absence of tubercle bacilli may lead to an erroneous diagnosis of malignant disease

Commercially prepared coccidioidin is available. It is prepared by dilution to the desired strength with sterile isotonic sodium chloride solution For sensitive patients, for instance those who are suspected of having coccidioidal erythema nodosum, a 1·10,000 dilution of the coccidioidin is advisable. However, 1.100 dilution may be used which may evoke a severe local reaction and even some systemic reaction, but there seems to be no great danger of causing dissemination of an active infection or flaring up of a quiescent one if a reaction ensues In suspected ancient infections in the presence of pulmonary cavities presumably coccidioidal, a final test with 1.10 dilution is made. Caution is necessary in interpretation because the cross reactions associated with histoplasmin sensitivity are increased with these stronger concentrations. As in the Mantoux test, 0 1 ml of the antigen is injected intradermally Readings are at 24 and 48 hours, and induration of more than 0 5 cm in diameter at either time is considered positive If only one reading is possible, that at 48 hours is preferable. The reaction is interpreted as in the tuberculin test

A negative result of a coccidioidin test, like a negative result of a tuberculin test, apparently rules out infection except in the patients with coccidioidal granuloma, who are frequently anergic.

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areas, for instance in the San Joaquin valley in California, parts of Arizona and New Mexico, and central west Texas. The morbidity rate in man follows closely a seasonal variation, most instances occurring in the dry months of summer and autumn when dust is most prevalent.

The usual portal of entry of *Coccidioides immitis* is the respiratory tract, but it can and does enter through abrasions in the skin. It is accepted that man becomes infected with coccidioidomycosis as a result of the inhalation of desert dust contaminated with chlamydospores of *Coccidioides immitis*. A parasitic stage in the life cycle of the fungus then occurs. It is believed that the saprophytic stage in the soil must then occur again before the fungus can be infectious to man because the disease is not transmitted from one human being to another.

Smith has reported, from evidences adduced from clinical observations, laboratory examinations and coccidioidin skin tests, that thousands of migratory workers in California have acquired coccidioides infection From the present evidence newcomers appear to be more susceptible to the benign infection than do natives or residents, who may have acquired a degree of immunity to the disease An investigation was made of 432 patients with "San Joaquin fever" in Kern and Tulare counties during the 17 months beginning December, 1937, which indicates the usual course, all recovered without sequelae.

The disease coccidioidomycosis occurs in two forms. (1) as an acute primary infection (valley fever) and (2) as a more chronic severe illness (coccidioidomycotic granulomatosis). Both sexes of all ages are susceptible

Valley Fever. After an incubation period of from 1 to 2 weeks the disease often begins with fever, generalized aches and pains. Soon there are skin manifestations resembling erythema nodosum, or occasionally erythema multiforme The cutaneous lesions are often associated with arthritis, sore throat and conjunctivitis As the disease progresses it may simulate the manifestations of bronchial pneumonia, tuberculosis, pleurisy, smallpox, measles, tularemia, syphilis and typhoid and occasionally poliomyelitis

The initial clinical manifestation may be an acute pneumonia indistinguishable from other types of pneumonia The physical findings and the roentgenographic evidence of pulmonary involvement may disappear promptly and completely as in an ordinary pneumonia However, in a considerable number of patients resolution of the pulmonic consolidation is slow The residual infiltrations consist of nodular densities, cavities, fibrosis and pleural effusion Characteristically these residual pulmonary lesions remain unchanged for months or even years The resemblance of the residual pulmonary lesions to tuberculosis is great.

Involvement of the joints in both benign and chronic types of coccidioidomycosis may occur The involvement may assume a mild form which usually subsides. In the serious phase of the disease the affected joints seem to be foci for dissemination of a generalized fatal infection

The joint manifestations are those of an acute or subacute bacterial infection.

Coccidioidal Granuloma. Coccidioidal granuloma in man is a chronic, progressive, highly fatal fungous disease affecting the lungs, skin, lymph nodes, bones, meninges, thoracic viscera and other body tissues. However, as in valley fever, it is probable that the initial lesion of coccidioidal granuloma is in the lung In contrast to the wide distribution of the lesions observed in man, the infection in cattle seems to be confined to the thoracic lymph nodes and the lungs.

Coccidioidal granuloma occurs more commonly among those who have dark skins than among those who have light skins.

Endogenous reinfection or dissemination at the time of the primary infection originates symptoms and physical findings of the more severe and usually fatal disease. This more fatal disease resembles disseminated tuberculosis. Lesions which are clinically indistinguishable from those of tuberculosis may appear anywhere in

the body, for example, in the lungs, larnyx, lymph nodes, bones, joints and central nervous system.

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18

THE ALLERGIC STATE

A definition of the term *allergy* as adapted from von Pirquet and Rolleston describes all forms of altered reactivity of the organism, whether, according to time, early, accelerated or delayed, according to quantity, exaggerated, [illegible] or abolished, or according to quality, color of [illegible] includes all forms of [illegible] allergy is the term [illegible] ity or extreme inse[illegible] to express the hypersensitiveness produ[illegible] to a foreign protein, and depends on an antigen-antibody reaction

The *allergic state* indicates a condition of a human being, in relation to his peculiar internal, constitutional reactions to certain specific external materials These materials excite specific characteristic symptoms when they are applied to the body or come in contact with the body of one who has this state of altered reaction The same external materials, when applied to the body or when contacted in the same amounts by normal persons, are innocuous to them These materials are known as allergens

Hypersensitiveness is the ability of a person to react with characteristic symptoms to the application of or contact with certain substances (allergens) in amounts innocuous to normal persons

THE ALLERGENS

An allergen is any substance which is capable of inducing allergy or specific susceptibility Allergens at times are designated by the terms sensitinogen and sensibilisinogen An allergen may be a protein or a nonprotein It may be a purified protein or a protein of some food, bacterium or pollen

In practice it is observed that allergens or allergic excitants comprise large and heterogenic groups of materials They cannot be classified, they may be grouped These various substances or groups of substances have been referred to in many categories to which allergens may belong (1) foreign proteins and their degradation products as by digestion or chemical change, (2) water-soluble and fat-soluble plant extracts and pollen oils, (3) chemicals of low molecular weights including some metals (atomic) such as nickel, (4) bacteria, viruses, molds, fungi and yeast and (5) physical agents, such as heat, cold and certain wavelengths of light Any one or even a combination of these heterogenic groups of substances in a predisposed and previously exposed individual may excite an allergic reaction

Some of the allergenic substances producing allergic states are antigens; others, such as pollen extracts, can be shown to exhibit some degree of antigenicity, and many obviously are not antigens It is for this reason that the term allergen or allergic excitant is used to designate them all. Many of the nonantigens combine with proteins or other substances of the host's tissues and assume thereby the nature of an artificial antigen

It has become important from the standpoint of diagnosis to remember that

either living or dead microorganisms or their products which may be used in diagnosis such as bacteria, viruses, molds, fungi, yeasts, or their soluble constituents or the egg mediums on which they are grown, and possibly certain of their metabolites, may be allergens. During an infection there may be a progressive invasion of the host and multiplication of the invading material and this material is an allergenic excitant. In some persons certain wavelengths of light and chilling (classed as physical allergens) cause reactions.

The materials which may give rise to the allergic states, and thereafter produce allergic reactions, as has been stated, are numerous. Common among these materials are foods, drink, particularly beer, foreign proteins and digestion products of these. Substances which may be found to be allergens are the water-soluble materials contained in pollens; pollen oils and other fat-soluble plant extracts, including urushiol from poison ivy, fat-soluble materials such as those which may be found in chocolate; chemicals and drugs of low molecular weight, such as formaldehyde, 2,4-dinitrochlorobenzene, paraphenylenediamine, mustard gas, quinine, aminopyrine, and sulfadiazine; and metals such as nickel

Sensitization is the ability of a person to react to an allergen with each contact. In certain allergies such as hay fever the *genotype* of the individual seems to exert control over the capacity for sensitization.

Sensitization may be the result of repeated exposures, and the necessary number of these varies among individuals and is indicative of differences in the host factors determining susceptibility to sensitization

The manifestations of allergy are multiple, varied, and distinct. These different reactions are manifestations of basic mechanisms with which the body is endowed These basic mechanisms respond by the production of specific substances to counteract the offense of specific offending matter. The recognition of the specific offending matter previously met with is accomplished by means of antisubstances The production of antisubstances (antibodies) in response to the specific offending matter (antigenic stimuli) is the antigen-antibody reaction.

In human allergies related to circulating antibodies, it seems that antibodies can be distributed unequally. An expression of this supposition is the term shock organ, which is used to distinguish the sites of predilection for allergic reactions, for instance, the bronchial mucous membrane (asthma), the mucous membranes of the eyes and the upper part of the respiratory tract (hay fever, allergic coryza or rhinitis), epidermal cells (eczematous reactions), the gastrointestinal mucosa (gastrointestinal allergy), or endothelium of the superficial vessels in the skin (urticaria, wheal-reacting allergies)

No human antibodies have been found accompanying certain of the human allergic manifestations, as, for example, allergy of the tuberculin type, contact dermatitis, and allergy to certain drugs It must be recognized, however, that this in no way invalidates the idea of fixed cellular antibodies in these instances. At the same time, it is observed that the agents responsible for these human allergic manifestations will not induce anaphylaxis in animals

Heredity is peculiarly important in the predisposition to development of allergy. However, heredity appears to be of no importance in the development of anaphylaxis. It is known that allergic diseases are not inherited as such. The allergic person inherits a predisposition or capacity to become sensitized and in consequence there develop unusual and specific reactions to certain allergens if sufficient contact with the latter occurs. The term *atopy* (meaning strangeness) is widely used to designate those conditions in which this hereditary tendency is recognized and which are mediated through the mechanism of atopic reagin Atopic disorders in this sense include hay fever, asthma, atopic dermatitis (eczema), angioneurotic edema and natural serum sensitiveness *Urticaria is not always* atopic. Allergic diseases which appear not to be influenced by the m

heredity and in which the reaginic mechanism is not demonstrable include contact dermatitis, bacterial allergy (tuberculin type), induced serum sensitiveness (serum sickness) and drug allergies.

TYPES OF ALLERGIC RESPONSE

Allergic reactions are of two types: the immediate type (for example, urticaria) and the delayed type (for example, tuberculin reaction)

Immediate Type. The reactions of immediate type become well developed soon after application or after adequate absorption of the corresponding allergenic substance, for instance as in asthma, hay fever and hives. In many instances of sensitivity of this sort circulating antibodies are demonstrable, and there is some accompanying cutaneous reactivity which assists in recognition of the allergen by means of a wheal-and-erythema response in the skin where the allergen is applied.

Local reactions to foreign proteins are transient in man. These local reactions are analogous to, and differ only in degree from, the Arthus reaction in the rabbit. Depending on the degree of sensitiveness and the availability of antigen, the patient will react within 15 to 90 minutes at the site of intracutaneous injection, with development of erythema and edema of variable degree.

The local inflammatory reactions which occur in anaphylactically sensitive persons are fundamentally similar to the foredescribed local reactions, and likewise the ability to react can be generally transferred by means of serum if the transfer is made to a person who has by heredity received a constitution which will permit the occurrence of allergic sensitization

Prausnitz and Kustner discovered that certain local skin reactions are transferable. In their work Prausnitz received in his skin a small amount of serum taken from Kustner, who was sensitive to fish or to foods containing fish Twenty-four hours later an extract of fish was injected into the site so prepared A local reaction developed in the course of some minutes and rapidly faded This technic was then extended and found to be applicable in many clinical allergies Whealing occurs at a sensitized site not only when the allergen is introduced locally but also when it is injected into remote tiss [illegible]

or [illegible]

spontaneous allergic states such as seasonal coryza and asthma, and with some kinds of eczema in those who are hereditarily disposed

The possession of reagins coexists with the presence of a corresponding clinical disorder The location of the principal reactive sites, shock tissue, determines the particular disease In some instances, however, reagins may be present in the circulation without manifest disease

The reagins or skin-sensitizing antibodies belong in the gamma globulin fraction of serum, are unduly heat labile, and possess as a distinguishing characteristic the property of sensitizing and remaining fixed in normal human skin for 6 weeks. During this period at any time a reaction may be had on the administration of an allergen The reaction occurs at the site of discharge, for instance, on the skin The reagins present in natural instances of hypersensitivity are not likely to precipitate the allergen unless the antibody is sufficiently concentrated. In instances of induced hypersensitivity reagins may appear in admixture with other, precipitating antibodies These naturally occurring reagins do not pass the placental barrier.

The clinical improvement from treatment of allergic patients by repeated injection of their own allergens is not produced by a diminution in the amount of their circulating reagins, but the injection gives rise to another, thermostable antibody, that is, to one that fails to sensitize the skin and withstands temperatures deleterious to reagins Normal persons under the same treatment give rise to the same antibody, but they do not produce reagin. This thermostable antibody com-

bines readily and specifically with the allergenic material, thereby neutralizing the latter so that a mixture of the two will not produce a positive cutaneous reaction on a sensitive person. The thermostable antibody is therefore termed the blocking or inhibiting or neutralizing antibody

The development of this [illegible] [illegible] body has been considered responsible for the clinical improvement, the [illegible] ment This assumption, however, has not been proved

Delayed Type. Reactions [illegible] ed type, on the contrary, require at least several hours after introduction [illegible] llergen before an effect is manifest. Such reactions may be illustrated by [illegible] the reactions caused by poison oak or poison ivy, most drug sensitivities and reactions to products of microorganisms for example tuberculin and histoplasm[illegible] These delayed reactions show progressive changes for 2 to 3 days or longer after contact or cutaneous administration.

Systemic Anaphylaxis. Anaphylaxis is an acute systemic reaction that i[illegible] exhibited by those in the hypersensitive state on subsequent injection of the same materials. This reaction comes on soon after the injection of the material and i[illegible] therefore of the immediate type. It has been observed in different species of animals and it is essentially the same regardless of the species or the antigen-antibod[illegible] system involved.

The mechanism by which anaphylactic shock is brought about is not full[illegible] understood According to current concepts, the important element is injury to th[illegible] tissues, particularly the vascular endothelium, either by antigen-antibody interac[illegible] tion or by *nonspecific materials such as peptone or serotoxins; subsequent* event[illegible] are determined largely by materials leaving the injured tissues Those who give a[illegible] immediate type of skin-testing reaction are the [illegible] system[illegible] accidents However, there are the early allergic [illegible] tion and the anaphylactic shock. There are ma[illegible] cause anaphylactic shock but cause variable degrees of symptoms. Such sympton[illegible] are termed *anaphylactoid reactions*

In the early or allergic inflammation type of response the dose of the allerge[illegible] is small. When relatively small amounts of antigen or allergen are introduced in[illegible] the tissues of a sensitive person, contact is localized, and the rate of absorption c[illegible] dissemination is retarded by tissue barriers and by existing antibody mechanism[illegible] The primary response of the tissues concerned is a local inflammation, initiated an[illegible] for a time kept stimulated by the allergic mechanism

In these hypersensitive persons small doses of the allergen may cause anaphy[illegible] laxis; in others larger doses of the allergen may be required to produce anaphylact[illegible] shock Anaphylactic shock is characterized by collapse, fall of blood pressure tachycardia, dyspnea of the asthmatic type, suffusion of the face, urticaria witl[illegible] giant wheals, and sometimes marked edema of the entire body In fatal instance[illegible] death may occur within a few minutes or as late as 24 hours after administratio[illegible] of the allergen

Systemic anaphylaxis may be observed under many circumstances. It may occu[illegible] immediately if the patient has had prior contact with the injected materials In other instances anaphylaxis may come on only after repeated injections of tetanus *toxoid and of a prophylactic preparation of alum-precipitated diphtheria* toxoid and pertussis antigen

Among persons who have become sensitized to foreign serum because of prior administration, those who have become so hypersensitive that on skin testing they give the immediate type of reaction are most prone to systemic anaphylaxis. In these cases the *histologic findings* are far more violent than in those of mild, transient inflammations. In other patients who have become very sensitive the specific reaction which ensues after the allergen is introduced into the tissue may be either an early or a delayed tuberculin type of reaction

The occurrence of the early type of local reaction coincides with the presence in the serum of antibodies that are capable of transferring corresponding sensitivities to normal persons.

When antigen is deposited in the skin or the subcutaneous tissues of anaphylactically sensitized animals, local allergic inflammatory responses start almost at once, with hyperemia and edema These reactions may be either frankly evanescent or more persistent If the reaction is more persistent and the skin becomes necrotic and sloughs, the state is termed the *Arthus phenomenon* (rabbit).

HISTORY

Elaboration of the principal complaint of a patient who has an allergy usually reveals other symptoms of allergic manifestation aside from the one from which relief is sought. These multiple manifestations emphasize that shock tissue in man is widely distributed throughout the body and that these different manifestations are the result of a single basic mechanism This concept, if kept clearly in mind during the interrogations necessary for history taking, permits an understanding of the different symptoms which may result from a single antigenic substance

It is well to know that in order for the foreign substances to reach the sensitized cell, either direct contact with cells on the surface of the body or with the lining of the respiratory and the alimentary tracts, or the passage of the substance through the blood or the lymph is necessary Direct contact of the foreign substance, however, may permit it to reach the blood stream by being absorbed from the skin, mucous membranes, or intestinal canal or from parenteral injection made as a preventive or therapeutic measure Once the allergic excitant reaches the blood, it will reach the shock tissues wherever they be situated The same symptoms therefore are produced whether the excitant is absorbed from the skin, the intestinal tract or the lungs. For instance, atopic dermatitis, urticaria, angioneurotic edema and other manifestations may result from absorption of naturally occurring protein or other allergic substance from the intestinal canal or the skin

The history may make clear the manifestations of allergy and, by so doing, renders other allergic symptoms, often bizarre and heretofore undescribed, recognizable and explainable with demonstration of an allergic mechanism in the production of the presenting symptoms

In eliciting the family history it is remembered that specific hypersensitivity is not inherited The development of a specific hypersensitiveness depends on a sensitizing exposure to the particular substance or substances to which the patient may be demonstrably sensitive The factors and circumstances which attend the development of natural specific hypersensitiveness (atopic) are obscure. An acquired sensitivity does not endure so long as a natural sensitivity Those who have sensitivity acquired as a result of a serum injection may be desensitized, while those having sensitivity of the natural or spontaneously acquired type cannot be.

The existence of a hereditary predisposition in both hay fever and asthma has been postulated and recorded by numerous observers Doerr-Basel has expressed the belief that the variation in the clinical manifestations of constitutional sensitiveness in allergy suggests that the capacity to become sensitive is present in all human beings but in different degrees For these reasons an inherited tendency is carefully sought for in the family history, for it is to be regarded as the most important factor determining the probable development of an allergic state in any individual.

Allergens are similar to infectious agents in that both have unknown but definite causes for their methods of entrance. Thus, in patients who have nasal manifestations of allergy due to pollen, the nasal absorption of the allergen plays probably the most important part in sensitization.

Age at Onset. The incidence of the manifestations of allergy is highest in the first 10 years of life From the age of 10 years to that of 50 years the rate of onset is about evenly distributed. About one half of those who have an allergy are made aware of it before the age of 50 years The distribution between the sexes is equal.

CLINICAL MANIFESTATIONS

At one time or another diverse disease states which are in reality manifestations resulting from the mechanism of allergy have been described as disease entities of obscure etiology

In allergies related to circulating antibodies the antibodies can be distributed unequally among the various tissues Any tissue having more than its share of antibodies is termed a shock organ. The term shock organ is used therefore to distinguish the sites of predilection for allergic reactions. Basically the mechanisms for the election of the sites of predilection for allergic reactions are not explainable.

The allergic response may or may not correspond to the portal of entry of the allergen Some allergens are inhaled, some are swallowed, others are injected, while still others are obtained by contact. A number of allergens such as those associated with the infections are formed in the body and are detected by the injection of the proper excitant The method or means of obtaining an allergen cannot always be determined, for indeed the offending substance may enter through all routes

The common clinical manifestations which often may be proved to be an allergic response are manifested in the skin as a dermatosis (including conjunctivitis and rhinitis), respiratory manifestations such as hay fever and asthma, and certain digestive disorders

Skin (Dermatosis). The cutaneous manifestation of hypersensitiveness of the skin, or dermatosis, may be of the immediate type (wheal-and-flare reaction) or it may be a delayed response

In practice it very frequently is difficult to know whether a particular cutaneous reaction is immediate or delayed in type Likewise it is often difficult to determine whether a particular dermatosis has been caused by contact with an allergen or whether the allergen has been inhaled or ingested.

Hypersensitive Cutaneous Reactions. For purposes of clinical description hypersensitive cutaneous reactions may be associated on the bases of the degree of reaction (1) the mild reaction consisting of erythema, (2) urticaria and (3) vesicles and bullae

Erythema Erythema is the mildest reaction and may occur as a punctate red eruption, as in scarlet fever, or as irregular reddened areas over various parts of the body There is no elevation of the temperature of the skin as there is in hyperemia The color may vary from light red to smoky purple. The colors are changeable, and may vary from time to time during the reaction With or without immediate changes of the coloration of the skin, urticaria may appear.

Erythema multiforme is a disease of young adults. It has a seasonal incidence in spring and fall Maculopapules, varying in size, pink, not scaly, and generally itchy, occurring on forearms, hands and face, are the main features of the disease Sometimes the eruption assumes a bullous form, and at other times there is an urticarial element.

Psoriasis, seborrhea, dermatitis and ringworm are differentiated mainly on the basis of the recent history, the distribution of lesions, and the absence of scaling. The differentiation from syphilis rests mainly on persistently negative serologic reactions

Flexural Prurigo. The lesions of flexural prurigo occur at the bends of the

elbows and the knees, and on the neck. They consist of papules and vesicles on areas of thickened, lichenified skin.

Dermatosis from Wearing Apparel. Dermatosis may arise from fabrics such as silk, wool, synthetic fabrics, leather, and artificial leather; from furs, rubber, and rubber-containing articles such as rubber gloves, dress shields and girdles, socks, pajamas, and brassières, and from metal alloys and plastics used in jewelry and in eyeglass frames, wrist watches and straps

Hypersensitivity to Naturally Occurring Fabrics. Schwartz and Peck have expressed the belief that an occasional dermatosis may occur because of hypersensitiveness to naturally occurring, unprocessed fabrics such as silk, wool, fur, or leather. Hypersensitiveness does not occur from linen and cotton fabrics However, a dermatosis may develop in those who pick flax, and from the oils of flax and cotton. (The oil of cotton is oleum gossypii seminis.)

Dermatosis may result from friction of a woolen garment when worn directly in contact with an actively moving part of the body This is not an allergic response.

Dermatosis from feathers in wearing apparel is very rare

Dermatosis among the wearers of furs may occur from the mechanical friction of the coarse hairs against the skin or from a sensitivity to the unprocessed fur However, although the chemicals used for tanning and dressing fur rarely cause dermatosis, in the majority of cases in which it occurs the dermatosis is due to dyes and tanning agents In order to cause sensitivity the furs must be so poorly dyed that the dyes are leached out by moisture Once sensitivity has developed, even a well-dyed fur may cause dermatitis The reduction of the incidence of dermatosis among the users of furs is in the hands of the dyers In recent years the dyers have been aware of this fact and have processed the furs with greater care than formerly so that now reports of such cases of dermatosis rarely appear The preventive measures used by the dyers include the use of weak solutions of the dyes, applied frequently or applied for longer periods, the careful oxidation of the dyes and the thorough removal of excess or unoxidized dyes by washing and drumming

Dermatosis among leather workers is due to the many primary irritants and sensitizers used in processing the hides to convert them into leather Dermatosis from hatbands, gloves, wrist-watch straps, pocketbooks and other leather articles has been reported. However, the incidence of dermatosis due to wearing and handling leather goods is small In the majority of instances due to contact with leather the dermatosis is of the allergic type The sensitizing chemicals may have been dissolved out of the leather by water or perspiration

Dermatosis may occur from artificial leather from the dyes, the resins, the formaldehyde, sulfur, the antioxygen and other chemicals used in the manufacture. The inner lining of shoes as well as the backing contains chemicals which may cause dermatosis The backing of shoes contains adhesives, antimildews and fungicides. In a number of instances artificial leather is used on the inside of the shoes

Hypersensitivity to Synthetic and Processed Fabrics. Most instances of dermatosis among the wearers of fabrics, according to the experience of Schwartz and Peck, is caused by the finishes rather than by the dyes Processed fabrics are made of cellulose (rayon) and of a number of plastics and other materials

The synthetic resin finishes have caused a number of cases of dermatosis. The completely cured resins do not as a rule cause dermatosis When complete polymerization and stabilization do not occur, there may be enough uncured resins remaining on the fabric to cause dermatosis in sensitive persons

Fabrics treated with tar or resins and rubberized in order to make them waterproof cause dermatosis only among the processors of the fabrics Canvas and leather gloves, sleeves and aprons used as a protection by welders cause dermatosis among the workers who process the fabrics but not among the users of these fabrics

Silicofluorides, chloronaphthalenes (naphtha balls), chlorobenzene, chlorophenols, and synthetic camphor used in mothproofing do not cause dermatosis.

The best known of the purely synthetic resin fabrics is nylon In all instances dermatosis from nylon is caused by a certain finish and not by the nylon itself.

Cases of dermatosis due to glass fabrics have been reported The dermatosis is due

to the resins or the mechanical irritation of the rather sharp fibers and not to allergy.

Glass wool for insulating purposes causes a mechanical irritation from the sharp ends of the broken glass threads and occasionally from sensitivity to the resin binder (phenolformaldehyde).

Rubber hydrochloride, vinyl resins, acrylic acid resins and cellulose acetate are laminated onto cotton or other natural fabrics in order to make them impervious. Dermatosis in all instances of exposure is due either to plasticizers or to stabilizers used in the films.

Rubber gloves, girdles, dress shields, gas masks, and condoms have all been reported to cause dermatosis In these cases the accelerator and antioxygen or compounds formed on the surface of the rubber by "vapor cure" (sulfur monochloride) were the actual irritants, not the rubber itself Dermatosis from "vapor-cured" rubber is caused by continuous changes taking place on the surface of the rubber, and these changes result in the formation of sensitizing chemicals Those who have dermatosis from wearing vapor-cured gloves (for example, surgeons) may prevent it by soaking the gloves in a 5 per cent solution of sodium carbonate for 15 minutes and then rinsing them in water, sterilizing by dry heat, powdering them well on the inside, and wearing them dry. The same procedure may be adopted by those sensitive to rubber gloves made from latex, because in such gloves the accelerators and antioxygen are easily leached out by perspiration

Several types of synthetic rubber used in wearing apparel may cause dermatosis Most of the dermatoses from synthetic rubbers probably are due to the same compounds that cause dermatosis from natural rubber, although synthetic rubber does contain sensitizing substances not present in natural rubbers

Dermatosis due to fabric dyes is relatively infrequent When dermatosis is caused by the dyes, it is usually due to an idiosyncrasy to the dye itself or to a faulty process of dyeing, so that there is retained in the fabric some chemical which should not have been present

When dyes themselves cause dermatosis, they "bleed" or come out of the fabric easily. Dye intermediates are more likely to cause dermatosis than the finished dyes themselves Under conditions such as the heat of ironing, some dyes will break down into their intermediates Wool is often dyed by the aid of a mordant Of the mordants it is the dichromates which cause dermatosis and not the dye.

Special acetate dyes are used for dyeing of rayon and these may cause dermatosis.

Dermatosis produced by jewelry in most instances is due to metallic jewelry containing nickel. Dermatosis can occur from some of the modern jewelry made from various synthetic resins, glass and casein The finished products and not the unprocessed material may give dermatosis.

The essential indication that dermatosis originates from wearing apparel is that the eruption begins at the place of contact with the offending material, usually 5 or more days after the garment has been worn The eruption may commence immediately if the person is already sensitive to the chemical in the wearing apparel which causes the dermatosis It is exceptionally rare for a generalized eruption to appear, but such may be the case, and sometimes systemic symptoms such as elevation of temperature may accompany the dermatosis These illnesses resemble serum disease or serum sickness

Bacterial Toxins. There are a few dermatoses which result from infections by bacteria which are known to produce toxins which irritate the skin during the course of the infection or which give a delayed type of cutaneous reaction Some of the special types of delayed reactions are used in diagnosis.

Streptococcids. Streptococcids are grouped miliary papular *eruptions occurring* during the course of streptococcal infections

Tuberculids and Tuberculous Dermatosis. Tuberculids or the lesions of tuberculous dermatosis do not contain tubercle bacilli, but although an active primary focus may not be evident, there is a positive reaction to the Mantoux test

The *papulonecrotic tuberculid* affects the follicles of the skin, producing a deep-seated nodular and occasionally necrosing lesion Lesions of this type may occur without evidence of active tuberculosis. Whether or not there is active tuberculosis

does not minimize the importance of distinguishing these lesions from those caused by syphilis.

Lichen scrofulosus is a round or flattened, small reddish yellow papule in an inflammatory patch occurring in a patient who has glandular tuberculosis.

Erythema induratum (Bazin's disease, tuberculosis indurativa) begins as hard, deep-seated nodules on the skin of the lateral and posterior aspects of the distal regions of the leg At first the lesions are light brown, which changes to light red The color may become darker, and the lesions soften and finally break down, forming ulcers which have abrupt edges. The disease is chronic, and when the ulcers or nodules heal, their former sites are marked by deeply pigmented spots. Definite evidence of tuberculosis elsewhere may or may not be present. Reaction to the Mantoux test is positive.

Erythema induratum is differentiated from erythema nodosum by the fact that in the latter the lesion does not ulcerate, does not show pigmentation, and the disease yields to salicylate therapy Varicose ulcer is accompanied by an evident varicosity of the veins. A satisfactory differentiation from syphilis is not possible.

Trichophytids, generalized papular eruptions, may occur in those who have ringworm If a positive reaction to trichophytin is present, it may be diagnostically helpful.

Erythema nodosum is associated with rheumatic fever and tuberculosis. Erythema nodosum occurs in two young women for each young man so affected.

The etiology of erythema nodosum seems to be uncertain, for some consider it a disease caused by a specific virus, while others consider it an accidental phenomenon of allergic nature in different diseases The occurrence of erythema nodosum in association with various drugs and the significance of sulfathiazole in children, mainly with reference to primary tuberculosis, seem certain Erythema nodosum can develop in association with treatment with other sulfonamides, but frequency is low compared with that associated with sulfathiazole therapy There is no difference between the lesions of spontaneous erythema nodosum and those of erythema nodosum following the administration of drugs, although in the latter the lesions clear up rapidly when administration of the drug is discontinued without passing through the color phases of the spontaneous type.

The concept that erythema nodosum is associated with tuberculosis is prevalent Holmdahl concluded that the primary infections seem to be combined with erythema nodosum to about the same extent during the various periods of childhood, with the exception of the first years of life Holmdahl followed 657 patients who had primary tuberculosis with erythema nodosum from birth to the age of 16 years The observed prognosis was least favorable in those who had primary tuberculosis with erythema nodosum in whom primary tuberculous changes were demonstrable and in whom the course of the primary changes or the rise in sedimentation rate was protracted.

The lesions are of various sizes, some of them from 1⅕ to 2⅖ inches (about 3 cm to 6 cm) in diameter They are raised above the surface, are of a bright reddish color, and appear to be inflammatory, they are smooth, glistening, and are exquisitely painful on palpation At first the nodules seem to be firm and deep-seated. Later they may fluctuate, but they do not contain pus Erythema nodosum always comes on suddenly, and very frequently the lesions are accompanied by constitutional symptoms consisting of fever and generalized aches and pains. The lesions slowly clear up but tend to recur until the general health has been restored.

Urticaria. Urticaria is a more intense reaction than erythema. The hyperemia, if present, goes immediately to actual exudation of serum into the intercellular spaces and there are raised patches of skin with central white raised zones These urticarial wheals may have areas of redness around them. The urticarial lesion is of

short duration, perhaps a few minutes. Successive lesions may follow, and the disease may last, continuously or intermittently, for weeks, and *in some chronic cases, for* year[illegible] If pigmentation occurs with the lesions, the condition is urticaria pigmentosa, a st[illegible] [illegible]tion

[illegible] llergic state However, the association of urticaria with stress[illegible] [illegible]en observed by many.

Graham and Wolf found that in every pa[illegible] who could be adequately studied there was one leading factor in precipitating hives. This was a *feeling of intense* resentment generated in situations in which the person believed that he was unjustly "taking a beating" but could neither fight nor run Thus in every case in the series reported, exacerbations and remissions of the disease showed a good correlation with a particular attitude toward situations of living but little or no correlation with anything else.

It is important, according to Graham and Wolf, to distinguish between resentment, the feeling so characteristic of these patients, and hostility. Resentment is "a feeling of indignant displeasure because of something regarded as a wrong or insult," while hostility is "a feeling of antagonism or enmity, employing a wish to take aggressive action " Resentment, of course, may lead to hostility, but it is significant that in persons who have urticaria it usually does not

Prurigo. When an urticarial wheal subsides, an itchy papule may persist, *urticaria papulosa.* Prurigo may be a continuation of urticaria papulosa. The term prurigo designates secondary changes which take place in the skin following and accompanying the urticaria papulosa The thickened skin in the affected region loses its elasticity and manifests disturbances of pigmentation Many places may show depigmentation, and others show increased pigmentation Interspersed between these regions there are the hard, subsiding papules, generally 2 or 3 mm in size The regional lymph nodes become enlarged

Urticaria Pigmentosa In urticaria pigmentosa wheals can be produced by trauma (rubbing the skin with the hand) The additional characteristic of the disease is the *appearance of pigmented macules and nodules The disease begins in early infancy* and usually ceases after puberty, however, it may continue into adult life

Vesicles and Bullae. Severe reactions to toxins are characterized by vesicles *and bullae Dermatitis and pemphigus are examples of such reactions*

Dermatitis Herpetiformis. This is a chronic intermittent disease, mainly of young adults, though it occasionally occurs in older persons The patient's general *health remains good The intensely itching cutaneous lesions consist of symmetric* herpetiform groups of vesicles on an erythematous base The itch in dermatitis herpetiformis is as intense as this sensation can be, and still this itch is relieved by scratching The patient may remove the lesion with the fingernails, preferring the pain thus produced to the intense itch When the vesicles are thus destroyed by scratching before the patient is seen by a physician, the diagnosis may be difficult because the typical vesicles cannot be observed Reliance is placed on the history of the vesicles and the occurrence of erythematous patches with excoriated spots situated symmetrically over the thorax and limbs Tearing of the skin by scratching leaves scars Untouched lesions heal without scars Healing of these lesions is often followed by a brown *pigmentation which will finally fade away*

The prognosis is good as regards life, but the recurrent character of the disease and its indefinite duration are not pleasant to contemplate

Pemphigus. The varieties of pemphigus, namely, pemphigus acutus, pemphigus vulgaris, pemphigus foliaceus and pemphigus vegetans, are all included in this group of toxic dermatoses (dermatitis herpetiformis and pemphigus). All are characterized by serous effusion into the epidermis, giving rise to bullous eruptions. General symptoms do not always occur In some cases severe toxemias develop; when these occur, the patients often die.

The lesion of pemphigus is a blister, tense and clear, rising from apparently normal skin but becoming turbid, with a red inflammatory areola at its base as it becomes infected. When ruptured, a red, oozing region is left, composed of the superficial layers of prickle cells. This rapidly dries up and the horny layer re-forms, leaving no trace of the lesion. All forms of pemphigus are accompanied by evidence of general toxemia, but in contradistinction to dermatitis herpetiformis, there is no itch

Pemphigus Acutus. Acute pemphigus is a dangerous and fortunately a rare disease It is a form of pemphigus known as butcher's pemphigus because of the relative frequency with which it formerly occurred in butchers In these cases there is a history of a cut followed by general symptoms and only 1 or 2 bullae. These lesions gradually increase in number, often become hemorrhagic, and toxemia sets in.

Pemphigus Vulgaris This is chronic pemphigus It begins as an acute pemphigus with a few bullae, usually not grouped There is slight itch or pain The bullae heal as others form elsewhere, and thus the disease continues for months. The process may clear, not to return, or it may recur after a period The mucous membranes of the mouth may be affected. If the disease recurs, the patient's general health suffers and death may result ultimately The lesions of the mucous membrane in the mouth, nose and pharynx prevent eating because of the intense pain

In young, healthy persons the disease often runs a mild course and clears up permanently In a person of 40 years of age or more there is a tendency to relapse, and each relapse is more serious than the original attack.

Pemphigus Foliaceus The term pemphigus foliaceus derives from the loose epidermis remaining after the bullae have been ruptured. Two varieties of pemphigus foliaceus occur, a primary form, and the other secondary to pemphigus vulgaris.

When firm slanting pressure is made with the finger on an area of apparently sound skin, the top layers of the epidermis will separate and slide along on the lower layers, leaving an exposed raw surface This skidding phenomenon of the epidermis is pathognomonic of pemphigus foliaceus. The mucous membranes are affected. As the disease becomes generalized, the hair and nails are lost The raw surfaces become widespread, especially over the flexures. Shortly prior to death this is truly a terrible disease.

The prognosis is poor In many cases, after a variable period of time, death ensues from pneumonia or septicemia

Pemphigus Vegetans. This disease affects the lips, mouth, axillae and pubes. The bullae rupture and on their bases arise vegetations, hypertrophic, painful lesions which refuse to heal. Like pemphigus foliaceus, the disease often is fatal

Mixed Dermatoses. There are unknown toxins which may cause an erythematous, an urticarial, or a vesicular or bullous eruption When the skin reacts in a nondescript way, the condition is termed a dermatitis or an eczema One, two or more of these responses may occur simultaneously and the response is then termed a mixed response

Eczema. The etiologic agent or agents responsible for eczema are unknown There are factors, such as irritation, which determine the onset of eczema A lesion is present on the skin, for instance, an area of contact dermatitis, which becomes infected by scratching, after which eczema appears Scratching is a factor in keeping eczema active

Eczema comprises many types of cutaneous lesions, depending on the reaction to a toxin These lesions are (1) erythematous, (2) urticarial, (3) papular, (4) pustular and, when regressive, (5) scaly

Eczema is characterized by commencing in the epidermis The reaction of the skin in eczema is not so great as in dermatitis A patient who has eczema may have a personal or a family history of allergy There may be a history that the progression of the disease is by acute exacerbations of the chronic process. Easy exhaustibility may occur just before appearance of the eruption Eczema often reaches its peak

of severity by repeated acute exacerbations separated by more quiescent periods, and may remain for a long time fluctuating at the peak. In time the disease slowly subsides, but during the period of regression there are still relapses. Some persons never get well. Fever is not a feature of eczema unless the skin becomes infected by pyogenic organisms.

Patchy Eczema. A chronic eczema consists of slightly raised, dull red patches, studded with crusts of millimeter dimensions over a circumscribed area of skin The chronicity of these patches is the characteristic of eczema. These lesions often are associated with anxiety, tension and worry, failure to relax, and resultant fatigue. A lessening of the anxiety coincides with disappearance of the eruption.

Generalized Eczema. A generalized eczema frequently starts from an irritation of a patch of chronic eczema. There is an acute exacerbation of the patch, say on one limb, manifested by becoming larger and spreading, and often having the appearance of urticaria as it spreads Then areas of eczema occur on various parts of the thorax, across the shoulders and the sacro-iliac region General symptoms may accompany these acute exacerbations

Respiratory Passages. As has been stated, the portal of entry does not necessarily determine the site of the shock organ. However, in respiratory allergic disorders the allergen usually is inhaled

Pollens cause many of the respiratory allergies They may be the cause of the recognized states of seasonal hay fever and asthma, or any other allergic ailment which is restricted to the seasons during which these occur, or they may become manifested in the presence or the handling of certain blooming house plants Likewise seasonal dermatitis and some urticarias caused by pollens have been definitely proved A patient sensitive to the pollen of tall ragweed, for example, is sensitive to all other ragweeds of the same genus as well as to closely related genera The same antigenic relationship appears to exist in regard to all members of other taxonomic groups

Dander from any hair-bearing or fur-bearing animal is potentially a source of allergen for predisposed persons. The relative importance of the respective members of this group appears directly proportional to the extent that conditions of contact are favorable to it

The *feathers* of geese, ducks, chickens, parrots, canaries, pigeons, sparrows, pheasants, and grouse have been known to cause asthma and vasomotor rhinitis. Feathers may also be the cause of cutaneous manifestations.

Although *dust* is omnipresent, not all types are allergenic. Occupational dusts of various types are important *House dust* is the commonest allergen of this type because of its universal distribution All types of dust, from road and field dust to those originated by occupations or industry, are present wherever man lives Not all of these are the means of production of allergic diseases. Some of these dusts produce disease by the presence of particulate matter

The *seeds* of cotton, kapok, and flax may be allergens. *Cottonseed oil* is a common food oil and fat Occasionally it is an allergen Kapok is used in the manufacture of mattresses, pillows, and furniture The oils of kapok, and occasionally of flaxseed, have uses similar to those of cottonseed oil.

Orris root is present in face powders, face packs, tooth powders and pastes, bath powders, scented soap, and perfumes and hair tonics Confectioners and bakers mix orris root with candies and pastries to impart the odor of violets Its use as a dry shampoo is common Tincture of orris is sold as a cheap violet perfume. Orris root is a very important source of allergens

Allergic disease of respiration is suspected in those who have symptoms of hay fever or asthma with or without an accompanying eczema, urticaria, or angioneurotic edema Respiratory allergic diseases often occur and are related to a known environment where there exist dusts of domiciliary or of occupational origin which are inhaled, or where there is contact with certain plants or chemicals and other suspected materials

An uncommon frequency of "colds," bronchitis or pneumonia in childhood suggests the existence of an early allergic stage.

The history of asthma, hay fever, or eczema among the relatives bespeaks a strong probability of allergic constitution of the patient This probability is proportional to the genealogic incidence and the proximity to the patient of allergic individuals in the family

Hay Fever. The symptoms of hay fever begin suddenly and often there is a punctuality in the date of annual recurrences There are the symptoms of severe coryza with moderate to profuse watery discharge The eyes are reddened and watery, with itching lids. The senses of taste, smell, and hearing are dulled and in some instances greatly impaired In some patients a cough may be mild, in others it is severe The cough is excited by a tickling sensation in the throat When symptoms are severe, there are chilliness, insomnia and poor appetite, which are soon followed by weakness. The symptoms vary from day to day and there may be attacks of bronchial asthma. The symptoms last just as long as the patient is exposed to the offending allergen

Allergic Bronchitis. Allergic bronchitis is a perennial or seasonal allergic reaction to sensitizing substances in a susceptible individual It is characterized by a chronic recurring or paroxysmal cough, which usually occurs in the absence of infection of the upper part of the respiratory tract or of intrathoracic disorder.

The primary symptom of chronic dry cough may be accompanied by blood-streaked sputum, expectoration of mucoid or mucopurulent sputum, wheezing, dyspnea, frequent colds, fever, fatigue, loss of weight, anorexia, thoracic pain, sweating, hoarseness, and aggravation of cough with exertion

Diagnosis is primarily the exclusion of all other possibilities A family history of allergy and other personal manifestations of allergy may indicate the diagnosis, but lack of them does not exclude it Most of the causative allergens are inhalants or caused from foods The high incidence of sensitivity to fungi and mold is probably indicative of strong antigens and also of a high incidence of epidermophytosis

The roentgenologic examination of the lungs is the most useful procedure in excluding organic disease of the lungs and pleurae Cardiovascular disease is considered and excluded. Most helpful is a history of similar attacks or other allergic manifestations

Asthma. Allergic asthma is a paroxysmal respiratory reaction manifested by an expiratory dyspnea of a noisy wheezy type

A working classification of allergic asthma has been made by Rackemann based on the assumption that asthma occurs in only those who have inherited the "asthmatic state" and that asthma due to extrinsic causes begins before the age of 30 years Asthma occurring after the age of 30 to 40 years is due to intrinsic causes.

The disease commencing before the age of 30 years is caused by something present in the environment, it is extrinsic In such case the symptoms come and go and are precipitated by, for instance, pollens, dusts, cosmetics, textiles, chemicals and animal products

Asthma which begins after the age of 30 years, particularly after the age of 40 years, is intrinsic asthma The cause is in the patient An occasional older patient will have idiopathic emphysema, cardiac asthma, or bronchial tumors, but many of them will have none of these things

These older patients will have nothing more definite than evidence of psychic or somatic stress or tension. To assign a psychic or emotional etiology for this group of patients is probably correct, but rarely is this the only cause for poor health Emotional disturbances which may be thought to be the cause of the asthma may be the result of the exhaustion from the repeated asthmatic attacks Abscessed teeth, nasal polyps, sinusitis, bronchitis, heart disease, diseases of digestion, urogenital disorders and malnutrition may precipitate asthma in a person who has inherited the allergic state. Once a person has had an asthmatic attack, the fear of more attacks is deeply seated and it may be difficult to give genuine assurance that death will not result from an attack of asthma, for indeed it may do so in rare instances

The disease has no sex preferences but affects the sexes differently during certain

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there being a fully developed attack of asthma. A cough beginning in the early hours before day which clears as the day passes may be attributed to asthma A cough which does not clear up as the day passes is due to chronic bronchitis on a nonallergic basis

The asthmatic attack develops by a slow increase in the cough and the wheezing in the thorax, and then the *paroxysmal stage* may be gradual or abrupt. In those who have hay fever, coryza, sneezing and lacrimation often precede the paroxysm. However, not all who have hay fever have asthma Attacks of asthma often may come with an acute infection of the upper part of the respiratory tract.

The cough in the earlier part of the attacks is short and unproductive, but increases and becomes more productive. In the severe attacks the dyspnea increases to orthopnea and the patient seeks to support himself in a semireclining position on the elbows and hands in order to utilize all the accessory muscles of respiration to the greatest advantage as an aid to getting more air out of the lungs

The prolonged attack or status asthmaticus frequently occurs as the result of conditions imposed on the patient. These patients are nervously overwrought and have been overmedicated and lack sufficient sleep, fluids and foods The patient has extreme, constant dyspnea of a wheezy nature as a manifestation of the continuing attack There are an unproductive cough, cold clammy skin, and cyanosis. There may be fever The pulse rate is rapid and may be irregular. The demand to breathe requires total effort Unconsciousness or disorientation may develop. The elevation of temperature in the presence of pulmonary signs may appear to be that indicative of pneumonia Such signs as consolidation and leukocytosis are characteristic of bronchial obstruction These patients, however, usually will develop a loose cough, and on expectoration of large amounts of mucus dyspnea will subside and the attack ends The duration of the attack varies from a few days to a week and occasionally longer. In status asthmaticus there is prolongation of the attacks or they are often repeated The paroxysm may be present for days and consequently no food, drink or sleep is obtained In these patients, in contrast to acute asthma of short duration, death may ensue.

The acute paroxysms of asthma which occur only after intervals of months do not cause deterioration of health As the disease progresses, the paroxysms become more frequent and are of longer duration, emphysema and a deterioration of health are inevitable results The excessive bronchial secretion is continuously present, occupying space in the bronchial system which should be filled by air. Cough, breathlessness and weakness are now chronically present.

Physical Examination. During the attack respirations are increased and difficult There are audible wheezing and prolonged expirations There are whistling, or sonorous rales heard throughout the lungs, *particularly in the expiratory phase.* The pulse is accelerated and in severe asthma is enfeebled. In the absence of complications cyanosis is not remarkable, but may be intense when moderately severe emphysema is present In the absence of secondary infection the sputum is clear and tenacious Eosinophil cells in the sputum are pathognomonic of asthma

Diagnosis The diagnosis is established by observation of the patient during the attack, for the paroxysm of asthma once seen is unforgettable The specific diagnosis in extrinsic asthma is established by finding the allergen or allergens which excite the disturbance The presence of eosinophil cells in the sputum is helpful diagnostically In the chronic stage of either extrinsic or intrinsic asthma the diagnosis is attended with more difficulty, since emphysema may cause severe dyspnea and it is often present Asthmatic attacks which occur only at night in the aging patient arouse the suspicion of an early left-sided heart failure.

The discovery of the causative allergens is the first essential to effective specific treatment. Since the inhalant allergens are more frequent causes and since hyposensi-

age periods. Before puberty boys are most commonly affected. From puberty to menopause women are most commonly affected. After the age of 50 years men have a greater morbidity rate than women. The incidence decreases with the racial darkening of the skin, and consequently it is said to be less common in the black race. The most important factor in the susceptibility to asthma is the exposure to organic dusts There is a definite increase in morbidity rates in all of those who are exposed to organic dust in their occupational duties.

In a survey conducted by the United States Public Health Service in recent years, asthma ranked fifth among all causes of disability.

There is no paucity of theories which have been offered to explain the paroxysmal seizure of labored breathing characteristic of asthma. Some of these theories are enumerated as follows. (1) the theory of spasm of respiratory passages, (2) the theory of anaphylaxis (allergic asthma), (3) the theory of edema, (4) secretory factor and (5) nonallergic asthma. There are various others. Not all of these theories are discussed here

The theory of spasm postulates an exaggeration of the normal expiratory contraction of the bronchiolar musculature. Inspiratory relaxation allows air to enter through the open bronchi and bronchioles into the alveoli where it is entrapped during expiration The proof of such a spasm is lacking, and if it were present, the cause for it is unknown. However, it has been thought that such a spasm of the bronchiolar musculature might be due to disturbances of innervation or of psychic control.

The demonstration of bronchial constriction in the anaphylactic reaction in the guinea pig suggests that a similar reaction might account for the asthmatic seizure in man Asthmatic seizures in man have been observed to follow the ingestion of certain foods, for instance, eggs It has been observed too that an application of an extract of buckwheat to the skin will cause asthma in certain hypersensitive persons.

The edema theory of the asthmatic attack attributes the symptoms of the attack to a swelling of the bronchial mucosa comparable to that of the nasal mucous membrane or the skin in angioneurotic edema

The presence of tenacious mucoid secretion adhering to the walls of the passages of the bronchi and perhaps occluding some of the smaller passages might account for the asthmatic paroxysm

This secretory mechanism has no more than a secondary role in the production of the acute paroxysm which can come on within a few seconds and end in a few minutes without any evidence of increased or decreased secretion.

There are considerable numbers of patients who have attacks of asthma which cannot be proved to be the result of an allergy

SYMPTOMS The asthma attack often develops insidiously and progressively In some instances, however, paroxysmal dyspnea seizes the patient with terrifying suddenness.

The time and the frequency of the asthmatic attacks due to a single allergen occur when contact is made with that allergen For instance, in asthma due to atmospheric pollen the attacks characteristically occur during the season of a particular pollen The asthmatic attacks due to less well defined or to unknown allergens have a tendency to be manifested at night, often after midnight. The nocturnal exposure to bedding containing feathers, cotton, wool and the dander of pets may be responsible in some instances but not in all. The nocturnal periodicity of the asthmatic attack due to pollen is difficult to understand because less pollen is inhaled during the night than during the day. Apprehension and fatigue are important predisposing factors for nocturnal asthma, for in some patients the sequence of events is a strenuous day, a few hours of rest and sleep and then being awakened by asthma

Some patients can predict when they are about to have an attack of asthma

filling of the lungs with air and creates a desire to breathe

times will recede without an ensuing attack A cough may occur nocturnally without

fever, migraine, vasomotor rhinitis and urticaria either before or at the time of the illness Some persons have suspected that the eosinophilia is of parasitic origin

Meyenburg, in 4 patients with Loffler's syndrome who had accidental death, found that the infiltrations were of pneumonic type with exudation into the alveoli and with eosinophilic infiltration of the pleura, alveoli and the interstitial tissue Meyenburg failed to demonstrate tubercle bacilli or *Ascaris* larvae in the pulmonary tissue.

Symptoms when present consist of fatigue, irritating cough, associated sometimes with pain in the chest and with scanty sputum. The presence of fever is not constant.

Exaggerated vesicular breathing and sibilant rales over the region of infiltration are the only physical signs. The eosinophilia ranges from normal limits to 50 per cent.

Repeated roentgenologic examinations reveal the distinguishing feature of the syndrome as emphasized by Löffler which is the fleeting, migratory character of the infiltrations. They may be extensive and irregular in shape, or small and round. They may be soft or dense, unilateral or bilateral, and they may involve the entire lung or be limited to one lobe. Breton stresses the fleeting, migratory and in some cases recurring character of the roentgenologic shadows. The attacks of asthma, which may accompany the syndrome, are not considered to be an essential feature of the syndrome. Loffler's syndrome is observed more frequently in allergic asthma than in other conditions. It is therefore much like chronic allergic pneumonia

Diagnosis is established by the characteristic changes in the lungs on roentgenologic examinations. Loffler's syndrome is attended by eosinophilia in the absence of pulmonary tuberculosis or mycotic disease.

Eosinophilic Granulomas of the Skin. Eosinophilic granulomas of the skin are the cutaneous manifestations in Loffler's syndrome in the form of persistent erythema multiforme In view of the frequent plaquelike involvement of the face, the disorder must be taken into account in the differential diagnosis of sarcoid

Gastrointestinal Allergy. The intestinal membrane is impermeable to certain colloids and does not generally permit unaltered proteins to pass There is some evidence, however, to suggest that small amounts of food protein can pass unchanged through the normal intestinal mucous membrane and enter the blood stream A protein thus entering the blood stream may create a hypersensitivity in the same manner as one reaching the blood stream through other mucous membranes or the skin

Cardiospasm, dysphagia, and discomfort and a feeling of constriction in the esophagus may be due to an allergic reaction. In patients in whom edema of the esophagus occurs as an allergic reaction, the edema often appears in minutes after the ingestion of the allergen

Pain, nausea, vomiting, distention, belching, pylorospasm, and hematemesis may occur in association with an allergic reaction Hematemesis which is caused by allergic edema is a diapedesis of blood which is controlled by epinephrine Edema of the gastric mucosa has been observed endoscopically in those who have an allergic state

Allergic reactions involving the colon are said to be manifested by pain, abdominal distention, constipation, diarrhea and bleeding. Eusterman observed pain simulating that of acute appendicitis which he attributed to food allergy reactions

Gastrointestinal allergy may be suspected as a cause of all acute dramatic episodes of abdominal pain, vomiting or diarrhea if the usual concomitants of organic disease and neurosis can be eliminated The suspicion of allergy is enhanced by the history of previous similar episodes if appropriate studies made at the time did not disclose organic disease. A dietary history may reveal the partaking of certain items of food just prior to the attacks. Attacks of gastrointestinal allergy may follow acute

tization with these may be successful, this method of treatment not only may be advisable but may be necessary in case of inability to separate the patient from the allergen

Many patients who suffer from severe asthmatic attacks, and some who have mild attacks, are fearful and apprehensive of succeeding attacks. The fear and apprehension may be of such degree that much assurance that death will not occur as the result of an attack of asthma is necessary to allay their apprehensions Mild asthma in a psychoneurotic person often is a total disability.

Allergic Pneumonia. Acute allergic pneumonia and chronic allergic pneumonia are described

Acute allergic bronchopneumonia is, according to Miller, Piness, Feingold and Friedman, a pneumonic or bronchial process in an allergic individual characterized by signs and symptoms indicative of bronchial obstruction and pulmonary infiltration with or without fever

SYMPTOMS The symptoms may appear during the course of a prolonged attack of bronchial asthma or may appear suddenly during a bad cold An unproductive, distressing cough may be the only symptom. In the seriously ill, tachypnea, noisy expiration and orthopnea are present

EXAMINATION. The skin is cold. There is no cyanosis The tonsils are enlarged but not inflamed. Lymphoid tissue, in excessive amounts, may be present On respiration there are retractions of the intercostal spaces Abnormalities of percussion resonance and of breath sounds if present are characterized by areas of hyperresonance, impaired resonance, changeable rales, and suppressed or accentuated breath sounds

DIAGNOSIS In a patient known to have an allergic state, who has the foregoing history and findings attended by evidence of a bronchial pneumonia on roentgenologic examination, an allergic pneumonia is suspected The diagnosis is not made unless no other cause for the pneumonia is found.

Chronic allergic pneumonia is characterized by infiltrative pulmonary reactions and by eosinophilic leukocytosis In many instances no symptoms of the disease are present and the condition is found during a routine physical examination and confirmed by roentgenologic examination. These pneumonias are generally the result of unknown and indeterminate allergens

When symptoms are present, they may be from the original disease, one which is prone to give allergic manifestations, or from a low-grade fever for which chemotherapy has been employed Weakness, cutaneous eruptions, anorexia, headaches and vomiting are due to chemotherapy and not due to the pneumonia

On general examination there is evidence of pulmonary consolidation There is often leukocytosis with marked eosinophilia

A continued fever associated with pulmonary infiltration in the absence of prostration in cases in which no likely etiologic bacterial or viral agent can be demonstrated, combined with leukocytosis and eosinophilia, is almost diagnostic of chronic allergic pneumonia There may be a relative increase in eosinophils in the sputum Clearing of the cutaneous and pulmonary findings following the discontinuance of drug therapy substantiates the diagnosis of allergic pneumonia

Löffler's Syndrome. Loffler described a syndrome characterized by transitory pulmonary infiltrations, eosinophilia, and a mild clinical course which was in contrast to the extensive pulmonary lesions as seen in the roentgenograms in his cases Some instances of the syndrome were discovered in supposedly normal persons in the course of mass roentgenologic examinations The illness is attended by an eosinophilia which suggests the allergic nature of the disease

Loffler first suspected that the disorder was a mild atypical form of pulmonary tuberculosis Maier reviewed 100 such cases and found only 2 patients who had active tuberculosis. Fifty-two of the 100 patients in Maier's series had eczema, hay

the family of the affected person are likewise susceptible. Therefore there are often both an individual and an inherited susceptibility. It is those who have this predisposition to enteritis who are affected most commonly by the ingestion of food and drink which act as irritants either by physical or by chemical means. A non-susceptible person eating and drinking the same food and drink will not be affected

Sudden changes in weather causing chilling or overheating of the body surface predispose the susceptible patient to "a bowel upset" In susceptible patients the drinking of cold drinks when the body is overheated is often followed by vomiting, intestinal cramps, and perhaps loose bowel motions Ascent to a high altitude (hill diarrhea) is a conditioning influence in susceptible patients

Reactions to Serum and Bacterial Products. The use of horse serum and egg products in the preparation of antitoxins and antiserums produces dangerous allergies Failure to test the sensitivity of the patient before the use of these substances has resulted in numerous accidents and occasionally death.

Serum Sickness (*Serum Disease*) Subsequent to an initial injection of foreign serum there is a latent period of from 1 to 18 days, but usually 7 to 10 days, after the injection of a serum or an antitoxin containing serum A local reaction appears at the site of the injection. Immediately thereafter general symptoms develop consisting of edema, pruritus, urticaria, and erythema in topographic areas or generalized Accompanying these cutaneous reactions there are malaise, headache, vomiting, fever, adenitis, albuminuria, arthralgia, and occasionally a truly allergic arthritis These symptoms usually disappear in a few days The allergic arthritis of serum sickness is the only surely proved form of allergic joint disease.

Clinical manifestations closely resembling serum disease can occur as a consequence of drug therapy, for instance, with the sulfonamides, the arsphenamines, and various antibiotics such as penicillin

The Nervous System in Allergic Reactions. Reaction of the nervous system to allergies is poorly understood. However, it is known that neurologic manifestations, usually lesions of the spinal nerve roots or peripheral nerves, follow the injection of serums for therapeutic purposes or, less commonly, for the purpose of producing immunity Cerebral symptoms, meningeal reactions and perhaps spinal syndromes may follow these injections When the allergic state is present, neurologic conditions, usually cerebral symptoms, may occur without the injection of any foreign protein Occasionally either acute ascending spinal paralysis or polyneuritis may follow the injection of foreign protein, especially typhoid vaccine, without any of the usual signs of allergy

There is little or no information available about the anatomic basis of these conditions Cerebral edema and multiple meningeal hemorrhages have been described in meningeal reaction arising in the course of treatment for meningococcic meningitis. It seems that peripheral nerves may be injured by the reactions from injections of serum There is in such cases a perineural edema However, radicular lesions may be connected with the meningeal reaction. Kennedy has expressed the belief that the cerebral symptoms that he has described are due to edema of the cerebral cortex. Experimental work has revealed that congestion and even minute hemorrhage in the nerves and spinal cord may be produced by violent allergic reactions

During the course of serum sickness or toward its termination signs and symptoms referable to the nervous system appear and rapidly reach their maximal intensity There is often severe reaction at the site of injection, and the entire arm or leg, as the case may be, is greatly swollen. The distribution of the paralysis is independent of the site of the injection, at least to a large extent, for brachial plexus palsy may follow the injection of the serum into the thigh. Frequently serum has never been administered previously.

Often the first manifestations are neuralgic pains which follow the course of the

infections, or injection of serum or vaccine, or may occur in association with migraine.

Allergic manifestations in the abdomen are often said to be related to intestinal dysfunction giving symptoms like those present in the so-called irritable colon syndrome. There is mucous discharge in the feces, and episodes of pain occur along the course of the colon. In an allergy affecting the colon there should be attacks of disruption of colonic function in which the symptoms begin abruptly in the absence of the common precipitating factors for the irritable colon syndrome.

Gastrointestinal symptoms are common in those known to be allergic, and gastrointestinal allergic reactions are occasionally the first recognizable evidence of an allergic state In the patient who has acute symptoms, such as severe abdominal pain or fulminating vomiting or diarrhea, resort cannot be had to time-consuming investigative procedures In the event of pain simulating that of an acute abdominal emergency, if the possibility of an allergic reaction is considered, the correct diagnosis may at times be made and unnecessary operation avoided.

Unlike the finding of a high percentage of eosinophils in nasal secretion which is apparently diagnostic of an allergic reaction rather than of infection, cytologic examination of the gastric, intestinal and rectal secretions has given little assistance in determining the etiologic basis of suspected gastrointestinal allergy

If parasitic infections and leukemia can be excluded, an eosinophilia is usually of allergic origin In some instances eosinophilia has been noted as following the ingestion of food to which patients are sensitive

Despite the unpredictable reactions the skin may give to sensitivity tests, these tests are employed in selected cases For diagnostic purposes in patients who have gastrointestinal diseases it is not often desirable to make skin tests until complete diagnostic studies have been made.

Because of the uncertainties of the specificity of skin tests, trial or so-called elimination diets in the diagnosis of gastrointestinal allergy have been employed The use of elimination diets in the diagnosis and treatment of allergy is sound, but obviously no standard diet can be universally applied. If one of the standard elimination diets is used, it will need to be modified in accordance with information obtained from the history of diet, skin tests, and the individual response of the patient

Food diaries often supply more diagnostic information than any other procedure which is used in gastrointestinal allergy. In order to obtain a food diary, the patient is required to keep a diary of the daily intake of food, and an attempt is made to find some relationship between the ingestion of a certain food and the occurrence of symptoms

The diagnosis of gastrointestinal allergy can be made with a much greater degree of certainty if the general rules for the diagnosis of allergy in any part of the body are adhered to, namely, (1) previous history of other allergic manifestations or a strongly positive family history, (2) the presence of other allergic manifestations at the time of the attack such as urticaria, angioneurotic edema, nasal or bronchial symptoms, and migraine, (3) history of exposure to a known allergen, (4) minimal physical findings in the presence of constitutional signs of shock, in the absence of abdominal rigidity or muscle guarding and rebound tenderness in patients who are not infants or aged persons and (5) the presence of eosinophilia When these diagnostic demands are fulfilled, the patient will have a marked amelioration of symptoms after an injection of epinephrine (0 5 to 1 ml. of 1.1,000 solution).

Acute Enteritis Due to Increased Susceptibilities. An acute enteritis due to an increased susceptibility is worthy of separate mention in connection with gastro- [illegible] of etiologic

a cutaneous reaction of the specific type results from bringing together the allergen and the reagin in the skin. This association of allergen and reagin produces histamine or a histamine-like substance in the tissues and wheal and flare ensue. The wheal, with a surrounding flare, or an erythema results from the histamine formed in the skin Skin tests are made by (1) direct or (2) indirect methods.

Direct Skin Testing. The principle of the direct method of skin testing is to effect contact between the allergen and the reagin of the skin of the patient under investigation. Various technics have been used for this purpose under the following descriptive terms: (1) scratch, (2) multiple puncture, (3) intracutaneous and (4) contact (patch test).

Materials for testing for hypersensitiveness to many of the naturally occurring allergens are available in the market as (1) dry powders, (2) pastes and (3) liquids. All of these prepared allergens are adaptable to scratch, multiple puncture and patch test technics Only liquid preparations are reliable for use in intracutaneous technics It is well to exercise care in preparing the dilutions of the allergens, especially for large doses, to obviate danger to the patient In rare instances, if dilutions of the preparations have been improperly calculated, not only may constitutional reaction occur, but death may ensue.

Scratch tests are performed by effecting an abrasion about ⅛ inch long (3 mm) just through the epidermis, being careful not to draw blood, with a sharp pointed instrument such as a needle Additional scr [illegible]
of the allergen are made in the follow [illegible]
(1) If the allergen is liquid (or a [illegible]
powdered preparation, apply 1 drop of tenth normal sodium hydroxide to the scratch, add powder with a blunt instrument, and mix. Reactions usually are fully manifested in 10 to 20 minutes. This method is very reliable in testing for sensitivity of such substances as dry pollen

The multiple puncture technic is performed by placing a drop of liquid allergen on the skin and with a needle making a number of punctures of the skin through the liquid allergen Controls for the scratch and multiple puncture technics are effective by employing in performance of the test the vehicle or solvent used in preparation of the allergen.

The intracutaneous technic requires the use of a fine needle and syringe The material is introduced intradermally This test is often employed in the presence of dermographia and thus, like the scratch test, may result in many false positive reactions. Controls for these tests are usually separately injected comparable amounts of a 1 per cent solution of sodium chloride

Positive skin reactions are expressed by the presence of a zone of erythema surrounding the test site. The degree of positive reaction is based on the size of the zone of erythema in comparison with the control or with the test site. When there is formation of an urticarial wheal at the test site, it is recorded The following signs are employed and are generally understood (−) negative; (±) doubtful, (+) weak positive, (++) moderate positive, characterized by wheal formation up to 0 5 cm in diameter; (+++) marked positive, with wheal formation up to 2.5 cm, with pseudopodia and large zone of erythema, (++++) a marked positive differing from (+++) only in its larger size The skin of the forearm is the site usually selected for testing. If the patient is hypersensitive to an allergen, an erythema may extend proximalward from the site of injection, and constitutional or generalized reactions may occur. If an unusual local reaction occurs, it is well to inject epinephrine (1 1,000), 0.1 to 0 2 ml, into the central aspect of the wheal as a prophylaxis

The *patch test*, properly carried out and interpreted, is the most practical method for demonstrating the actual cause of a contact dermatitis It is employed by reputable manufacturers of wearing apparel to determine the possible skin-irritating or skin-sensitizing properties of the materials used (containing new chemicals) before placing the garments on sale.

Patch testing with strong concentrations of known primary irritants will result in reactions on any skin This does not mean that patch tests should not be performed with dilute solutions of chemicals which, in strong concentration, are known to be

spinal nerve roots. These pains are commonest in the arms and shoulders and may be unilateral or bilateral. Symptoms of meningeal irritation such as cervical rigidity, Kernig's sign and hyperesthesia are common. The nerve trunks are sensitive to pressure. Soon weakness or paralysis of the muscles appears and atrophy develops rapidly Often the muscles innervated by the fifth and sixth cervical segments are affected. The deltoid, spinati, rhomboids, biceps, brachialis anticus, brachioradialis and often the supinator and extensor muscles of the wrist may be partially or completely paralyzed. In rare instances, only the lower roots of the cervical plexus are affected. Paresthesia and hyperesthesia are present If the paralysis is extensive, small areas of hyperesthesia and analgesia may be detected

Lesions of the peripheral nerves are often but not always bilateral and symmetric The nerves most commonly involved are the radial, sciatic, peroneal, tibial, thoracalis longus and the axillary.

Occasionally there is a polyneuritis with emphasis on sensory phenomena.

A *meningeal reaction* occurs in those who have serum sickness Often these reactions are of an allergic type after intraspinous treatment with serums Deafness may be associated with serum sickness.

The essential features in diagnosis of allergic involvement of the nervous system are the history of injection of serum from 5 to 12 days before and the development of generalized signs of serum sickness just before the appearance of the neurologic manifestations

EXAMINATION

Both topographic and general examinations are performed The nose and throat abnormalities which so frequently accompany allergic conditions of the chest often require the services of the specialist, but not the specialist who calls all rhinitis "allergic rhinitis" The specialist describes the characteristic allergic nasal mucous membrane as being swollen, boggy and pale with a grayish or bluish color The gray color is due to generalized epithelial hyperplasia which is the essential feature of polyp formation Polyp formation is considered by many authorities as pathognomonic of allergy It is important to recognize also that allergy involves the sinuses as well as the nose

It is well to know that the roentgenologist cannot distinguish the true etiology of an edematous process from an infiltrative process, nor can he distinguish the etiology of one infiltrative process from that of another. Allergic pneumonia and allergic bronchial pneumonia, therefore, cannot be distinguished from other conditions producing similar shadows It has been shown that the edema due to allergy in the sinuses may at times be sufficiently great to produce shadows comparable with those of empyema

An endoscopic examination may be desirable, and if so the services of a bronchoscopist may be necessary for a complete diagnosis of the pulmonary condition, for even though asthma be demonstrated, an asthmatic patient may have some other pathologic condition which can be definitely determined only by this procedure

The presence of eosinophil cells in the blood in excess of 300 per cubic millimeter is considered abnormal. An eosinophilia is characteristic of allergy, but is not necessarily pathognomonic, for eosinophilia may result from blood dyscrasias which have been grouped under the term lymphogranulomatosis These blood diseases [illegible] as from the nose

[illegible] ic patients contain potential shock tissue. In order to detect the presence of this shock tissue, advantage is taken of the fact that these patients have shock tissue or potential shock tissue in the skin irrespective of the situation of the shock organ. It is postulated that

In cases of dermatitis suspected to be caused by elastic girdles and dress shields, patch tests should be performed with the rubber in the thread as well as with the fabric.

In testing with jewelry, first test with the suspected material itself. To test for nickel sensitivity, a 5 per cent solution of nickel sulfate is employed.

It requires considerable experience to interpret correctly reactions to patch tests The gradations of the reaction are the same as those for the scratch, the puncture or the intradermal methods and are recorded by the symbols 1+, 2+, 3+ and 4+. By this method an erythema on the area of skin to which the chemical was applied is indicated by 1+; erythema and edema by 2+, and an erythema, edema, papules and a few vesicles by 3+. Erythema, edema, many vesicles and in some cases ulceration are recorded as a 4+ reaction.

The degree of reaction will be greatest at the site of greatest concentration It is for this reason that weak concentrations of sensitizers must be left on longer than strong concentrations. They should be observed for at least 5 days after the patches are removed A reaction not present when the patch is removed but which becomes manifest less than 5 days after the patch is applied, is considered a delayed reaction. The delayed reaction indicates that a low degree of specific sensitivity is present or that a weak concentration of the sensitizer was used To report a patch test reaction properly, there should be given (1) concentration of the chemical tests, (2) amount of the chemical used, (3) area of skin contacted, (4) site of application, (5) number of days patch was left on and (6) periods after removal of the patch on which the readings were made. In this way a comprehensive appraisal of the reaction in terms of the degree of sensitivity can be made.

The true allergic reaction, as a rule, increases rather than decreases in intensity for 24 to 48 hours after the patch is removed Reactions of primary irritation with few exceptions tend to subside after the removal of the irritant

The evaluation of a weakly positive reaction (1+) depends a great deal on the observer's experience In dealing with a fabric or other substance containing a weak concentration of a sensitizer, a 1+ or 2+ reaction is significant.

The Intradermal Test. The intradermal test is most successfully employed for bacterial toxins, as in the Mantoux test, in which the reaction to varying doses of the toxin can be observed Other substances, such as pollens, are tested in this way by injecting them intradermally Certain substances are tested by placing the suspected agent into cross hatches or punctures made into the epidermis, as in smallpox vaccination A positive reaction is manifested by an urticaria shortly afterward, from one half hour to 1 hour usually, but in some instances, as in the Frei test (granuloma inguinale), 72 hours

Indirect Skin Testing. Indirect skin testing is an application of the Prausnitz-Kustner phenomenon, the passive transfer test (p 1323). The principle of this test is based on the transfer of atopic reagins in the patient's serum to local areas of the skin of a nonallergic person upon whom the test will then be made This passive transfer of sensitivity may be accomplished with either serum or plasma of the patient's blood A testing spot is usually selected on the back of the recipient; 0 1 ml of the patient's plasm or serum is introduced into a number of sites, depending on the number of materials to be tested After a period of 12 to 24 hours, and not until the traumatic reaction of the transfer injection has subsided, these areas are tested by the intradermal technic. Resulting reactions are similar and are recorded in the manner described for direct testing This procedure is not to be regarded as a routine, but it is most useful under certain circumstances Patients may present dermatitis so extensive as to preclude direct skin testing. The procedure may be desirable in the case of very young patients also.

The ophthalmic (eye) test is used most frequently in the determination of serum sensitivity when heterologous serum is to be used prophylactically or therapeutically. Reaction consists of hyperemia and itching of the conjunctiva accompanied by lacrimation A positive ophthalmic reaction indicates a higher degree of constitutional sensitivity than does a positive skin reaction A positive ophthalmic reaction contraindicates the injection of the serum or at least is an indication for the exercise of extreme caution.

Interpretations of Allergic Responses. A patient may exhibit a positive skin reaction to an allergen which provokes no symptoms when the allergen is other-

primary skin irritants These primary irritants can usually be removed from fabrics and therefore the chemicals which are not primary irritants are responsible for the great majority of cases of contact dermatitis caused by wearing apparel, cosmetics and ornaments. These nonprimary irritants induce a specific skin allergy and thus cause dermatitis. They are cutaneous sensitizers; that is, agents which do not necessarily cause demonstrable cutaneous changes on first contact but which may effect such specific changes in the skin that it will react after 5 to 7 days or more. Future contacts with the same materials will produce similar reactions or cause dermatitis on the same or other parts of the body

The patch test when used for diagnostic purposes consists in applying a small portion of the suspected substance to a site of normal skin of the patient. This is covered with innocuous impermeable material, which is then sealed to the skin by adhesive plaster There have been many modifications proposed in order to overcome certain objections.

The diagnostic patch test is performed by Schwartz and Peck in the following manner. If a liquid is to be tested, saturate a piece of four-ply gauze ¼ inch square and apply it to uninflamed skin on the arm or the back The liquid from the gauze should not be permitted to escape from the patch site. For insulation a 1 inch square of nonwaterproof cellophane is used This is sealed to the skin with adhesive plaster about 2 inches square. The reactions which may result from the adhesive plaster are separated from those resulting from the test substance by the uninflamed skin which is in contact with the cellophane only In performing a number of patch tests, care should be taken to avoid overlapping of adhesive plaster

If a powder is to be tested, the powder is placed on a moistened piece of gauze in order to keep the reaction localized

When solids insoluble in water are to be tested, they are dissolved in the solvent used in preparation for their use in the fabric A piece of gauze is then soaked in a saturated solution of the material In order to eliminate the action of the solvent the gauze is then allowed to dry before being placed on the skin.

When the insoluble solid is of a resinous nature, the solution may be painted directly on the skin, the solvent allowed to evaporate, and the cellophane and the adhesive plaster then applied If the resin adheres firmly to the skin, it is not necessary to cover it with cellophane and adhesive

It is usually sufficient to leave the patch on for 24 hours Sometimes, however, when testing with low concentrations or with weak sensitizers, it may be necessary to leave the patch on for several days, but not for more than 5 days, since the patient may by that time become sensitized to the patch itself The reactions are read on the removal of the patches every day for 5 days thereafter Reactions occurring at longer intervals after patching indicate a lesser degree of sensitivity than an early reaction.

A convenient way to test fabrics is accomplished by using a piece of the fabric about 1 inch square and applying it as a patch The reaction is observed each day up to 3 days, and after the removal of the patch at the end of 5 days. If the reaction is negative at the end of 5 days, the site should be inspected once more at the end of 1 week All patches are removed as soon as a positive reaction is obtained. Best results from a patch test are obtained while the dermatitis is still present

In patch testing with fur, the test should be carried out with the hairy side of the fur applied to the skin of the patient.

The first determination to be made when a patient is to be tested with leather, is whether the leather is real or artificial This can often be determined by tearing the [illegible]
fabric. If [illegible]
ance To [illegible]
perspiration [illegible]
to something in the leather

In investigating a shoe dermatitis, patch tests should be made with the backing In some instances the leather on the inside of the shoe, such as the tongue, the inner sole and the sock lining, may be the cause of the dermatitis, but rarely if ever the outside leather. The chemical which causes the dermatitis must get through the sock or stocking Therefore first patch test with the sock or stocking (before washing)

In patch testing with sponge rubber, test with both the spongy and smooth surfaces

In cases of dermatitis suspected to be caused by elastic girdles and dress shields, patch tests should be performed with the rubber in the thread as well as with the fabric.

In testing with jewelry, first test with the suspected material itself. To test for nickel sensitivity, a 5 per cent solution of nickel sulfate is employed

It requires considerable experience to interpret correctly reactions to patch tests The gradations of the reaction are the same as those for the scratch, the puncture or the intradermal methods and are recorded by the symbols 1+, 2+, 3+ and 4+. By this method an erythema on the area of skin to which the chemical was applied is indicated by 1+; erythema and edema by 2+, and an erythema, edema, papules and a few vesicles by 3+. Erythema, edema, many vesicles and in some cases ulceration are recorded as a 4+ reaction.

The degree of reaction will be greatest at the site of greatest concentration. It is for this reason that weak concentrations of sensitizers must be left on longer than strong concentrations They should be observed for at least 5 days after the patches are removed A reaction not present when the patch is removed but which becomes manifest less than 5 days after the patch is applied, is considered a delayed reaction. The delayed reaction indicates that a low degree of specific sensitivity is present or that a weak concentration of the sensitizer was used To report a patch test reaction properly, there should be given (1) concentration of the chemical tests, (2) amount of the chemical used, (3) area of skin contacted, (4) site of application, (5) number of days patch was left on and (6) periods after removal of the patch on which the readings were made. In this way a comprehensive appraisal of the reaction in terms of the degree of sensitivity can be made

The true allergic reaction, as a rule, increases rather than decreases in intensity for 24 to 48 hours after the patch is removed Reactions of primary irritation with few exceptions tend to subside after the removal of the irritant

The evaluation of a weakly positive reaction (1+) depends a great deal on the observer's experience In dealing with a fabric or other substance containing a weak concentration of a sensitizer, a 1+ or 2+ reaction is significant.

The Intradermal Test. The intradermal test is most successfully employed for bacterial toxins, as in the Mantoux test, in which the reaction to varying doses of the toxin can be observed Other substances, such as pollens, are tested in this way by injecting them intradermally Certain substances are tested by placing the suspected agent into cross hatches or punctures made into the epidermis, as in smallpox vaccination A positive reaction is manifested by an urticaria shortly afterward, from one half hour to 1 hour usually, but in some instances, as in the Frei test (granuloma inguinale), 72 hours

Indirect Skin Testing Indirect skin testing is an application of the Prausnitz-Kustner phenomenon, the passive transfer test (p 1323) The principle of this test is based on the transfer of atopic reagins in the patient's serum to local areas of the skin of a nonallergic person upon whom the test will then be made This passive transfer of sensitivity may be accomplished with either serum or plasma of the patient's blood. A testing spot is usually selected on the back of the recipient; 0.1 ml of the patient's plasm or serum is introduced into a number of sites, depending on the number of materials to be tested After a period of 12 to 24 hours, and not until the traumatic reaction of the transfer injection has subsided, these areas are tested by the intradermal technic. Resulting reactions are similar and are recorded in the manner described for direct testing This procedure is not to be regarded as a routine, but it is most useful under certain circumstances. Patients may present dermatitis so extensive as to preclude direct skin testing The procedure may be desirable in the case of very young patients also.

The ophthalmic (eye) test is used most frequently in the determination of serum sensitivity when heterologous serum is to be used prophylactically or therapeutically. Reaction consists of hyperemia and itching of the conjunctiva accompanied by lacrimation A positive ophthalmic reaction indicates a higher degree of constitutional sensitivity than does a positive skin reaction A positive ophthalmic reaction contraindicates the injection of the serum or at least is an indication for the exercise of extreme caution

Interpretations of Allergic Responses. A patient may exhibit a positive skin reaction to an allergen which provokes no symptoms when the allergen is other-

wise encountered. A skin sensitivity to a specific reagin may be present without clinical sensitivity to that substance. A patient may have definite sensitivity, in a shock organ, to an allergen without there being skin sensitivity to that substance *Negative cutaneous reactions in the* presence of specific reagins and allergens are less frequent than positive reactions which have no significance.

A positive skin reaction to dander of a dog or a cat in a patient who has asthma becomes significant when the removal of the house pet brings relief. A positive skin reaction due to the products of hens' eggs is significant when a dermatosis is relieved by an egg-free diet. When there are multiple positive cutaneous reactions, which is usually the case, an environment simultaneous free of all allergens for which positive cutaneous reactions have been obtained is attempted. If this procedure results in relief, contact may then be renewed with the suspected causes singly or in groups with deliberate intention of reproducing the symptoms. When it is feasible, such causes, if proved to be of clinical significance, are eliminated permanently. Those proved not important may then be restored

The history which suggests that an illness is referable to the allergic state is diagnostically important despite a failure of skin tests to confirm such an implication. A trial of eliminating the suspected allergens from the patient's environment is in order to effect a diagnosis

Some patients may be relieved by geographic change Such a change may involve many factors, such as disposal of pets and of articles of furniture, and other factors too numerous to mention or too obscure for recognition. In such instances, when change has effected a relief of symptoms, an inhalant allergen is indicated, especially when a return to the previous environment results in recurrence. Geographic change from a district where certain pollens are present to a district free of these offending pollens will give relief from symptoms such as hay fever and asthma.

The principle of elimination has been widely employed among patients who are suspected of being sensitive to foods but who give negative reactions to skin tests In applying the principle to foods, Rowe, whose plans of elimination are still used extensively, first popularized elimination diets. The elimination diet consists of lamb chops and rice Once the patient is established on the diet suspected articles of food are added and the results are observed

Certain specific allergic reactions require several hours to become manifest after the test material is deposited in or on the tissues These reactions exhibit no demonstrable relation to circulating antibodies, and the ability to react cannot be transferred by means of serum. When a substance which will cause this sort of reaction in the skin of a susceptible person is present, often only the epidermal cells react In other instances the deeper layers of tissue are involved The epidermal reactions of eczematous type present macules, papules, or vesicles, with hyperemia and itching. A sensitiveness manifested in the deeper layers of the skin results from invasion of the body by a variety of infective agents such as bacteria, viruses, fungi, and parasites, or from the use of drugs These allergies are designated simply by adding the term allergy to the name of the offending agent, for instance, *bacterial allergy*

The best known example of bacterial allergy or reaction of a delayed type is the tuberculin-tuberculosis relationship.

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Skin testing for the detection of evidence of the presence of acqu...

sensitization to the living agents of disease during the course of acute, chronic and clinically unrecognized infections or infestations have been successfully employed for: (1) tuberculosis, brucellosis, tularemia, glanders and soft chancre, (2) lymphogranuloma venereum and mumps and (3) the dermatophytids, coccidioidomycosis, sporotrichosis, histoplasmosis, echinococcus, trichinosis, filariasis, schistosomiasis and leishmaniasis.

Equivocal skin testing occurs in the presence of acquired allergic sensitization due to many and diverse disease agents, for instance, in bacterial focal infections, dermatophytosis, moniliasis, filariasis, schistosomiasis, ascariasis, enterobiasis, uncinariasis, leishmaniasis and trypanosomiasis

All bacterial infections show some degree of delayed-type reactions when extracts of the corresponding bacteria are put into the skin; such extracts may at times give immediate-type reactions as well, particularly in relation to a content of specific polysaccharides Usually these reactions are less pronounced than in the tuberculin-tuberculosis relationship.

Thus, when large samples of the population are tested with culture filtrates of a group A streptococcus (Dick test), there is found to develop with age a gradually increasing incidence of sensitivity and, superimposed upon this whenever diseases intimately associated with streptococci occur, a sharp rise in the number of reactors

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In infections by fungi useful diagnostic information can be obtained In coccidioidomycosis, on skin testing with coccidioidin (an extract of ground, heated culture growth), evidences of local or of general systemic reactions may be observed In histoplasmosis, local or general reactions are obtained with histoplasmin. In trichophytosis various preparations of trichophytin have been used with variously reported specificity of results of diagnostic importance.

Delayed-type reactions have been secured with certain viral materials. The skin reaction shown in smallpox-immune persons by killed vaccinal virus is an example The Frei test has been used diagnostically in cases of lymphogranuloma venereum.

The skin reactions of the host when tested with extracts of the body substance of the same or related parasites may give certain diagnostic indications in parasitic helminth infestations, such as in schistosomiasis, echinococcus disease, filariasis, trichinosis, and ascariasis These reactions are the immediate or the wheal-and-erythema type of reaction However, skin testing in this manner lacks sufficient specificity for routine employment for diagnosis of the same or related parasites Antibodies can usually be demonstrated in the serum by serologic methods in the positive reactors Asthma and rhinitis are sometimes elicited upon exposure to the specific agents While there is often an early reaction to hydatid fluid in echinococcus infestation, it appears that the delayed type of reaction should be given chief diagnostic interpretation.

In protozoan infestations only leishmaniasis seems to yield a tuberculin-like reaction which can be interpreted as being definitely useful diagnostically

As an aftermath of sensitization by insect bites and stings, delayed allergic reactions have been demonstrated independently of early reactions which occur at times; both varieties of reaction, however, may be seen in the same person

In general, when the method of skin testing is specific, in the presence of bacterial, viral and higher plant and animal infections such tests have a significance similar to that of tuberculin, a positive reaction denotes the occurrence of infection but gives no reliable indication of current activity It is most informative when

wise encountered. A skin sensitivity to a specific reagin may be present without clinical sensitivity to that substance. A patient may have definite sensitivity, in a shock organ, to an allergen without there *being skin sensitivity to that substance.* Negative cutaneous reactions in the presence of specific reagins and allergens are less frequent than positive reactions which have no significance.

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The best known example of bacterial allergy or reaction of *a delayed type* is the tuberculin-tuberculosis relationship.

When diluted tuberculin is injected into the skin of the tuberculous patient, *there is* [illegible] *at the injected* [illegible] nsity [illegible] the [illegible] patient allow of a *severer reaction,* there are central blanching and the [illegible] lopment of an innermost *livid* zone which may become necrotic The inflammation then slowly fades, but the *lesion* is palpable for some days and pigmentation may be observed for several weeks thereafter.

Skin testing *for the detection* of evidence of the presence of acquired allergic

nodosa, rheumatic fever, pneumonitis, disseminated lupus erythematosus, and rheumatoid arthritis. Whichever anaphylactic event occurs in a given animal is referable primarily to individual predispositon and the peculiarly elective sites in which either *the antigen becomes fixed or the antibody is produced.* Despite many analogies in the diseases so produced and those naturally occurring in man, the thesis is not proved that these diseases or even some instances of them are referable to sensitization, for the variety of reactions which tissues exhibit is very limited and the response of tissues to injuries of different origin may be similar

The studies of Rich and of other recent workers suggest that anaphylactic reactivity in man may at times be prominent in only a particular tissue.

At the present time it seems reasonable to assume that some sort of mechanism such as a chronic anaphylaxis is etiologically important in the origin of certain diseases.

Periarteritis Nodosa. Periarteritis nodosa is a rare disease, of unknown etiology, of the medium-sized and small arteries and arterioles.

Rich stated reasons to believe that the arterial lesions of periarteritis nodosa are dependent on increased sensitivity of tissue to foreign substances He reported a series of cases of serum sickness and reactions to sulfathiazole in which the lesions of periarteritis nodosa were found.

The condition belongs to the group of diseases now designated as collagenic diseases. Acute rheumatic fever, erythema nodosum and rheumatoid arthritis are examples of such diseases *The disease usually affects those between the ages of 20* years and 40 years.

The essential pathologic change is the localized necrosis of the medial coat of many of the arteries followed by exudation, necrosis, aneurysms and thrombosis In a few cases small aneurysms may rupture and cause hemorrhage or hemorrhagic extravasations In rare instances multiple aneurysms are present and give rise to beadlike lesions palpable along the course of the vessel.

Periarteritis nodosa is often like an infectious disease. There may be chills, fever, emaciation, marked and progressive weakness, insomnia and headaches, generalized muscular pains, peripheral neuritis, anorexia and various gastrointestinal disturbances. A rather characteristic feature of this disease is that during a period when there is no fever and the patient is generally comfortable and improvement should be had, the patient does not improve, but becomes weaker, more anemic and emaciated Subcutaneous hemorrhages, urticaria and purpura are common. Attacks of asthma may supervene. Instances of the disease simulating fibrositis may occur.

The disease may be difficult to separate from acute nephritis or hemorrhagic nephritis Fatal renal hemorrhage may occur Arterial hypertension and cardiac failure on the basis of coronary or hypertensive heart disease may appear to be the common variety developing a rapid course The central nervous system is involved in a few cases There may be symptoms of peripheral neuritis, even including the cranial nerves Abdominal pain accompanied by indefinite gastrointestinal symptoms may be the sole complaint.

There are no clinical findings solely indicative of periarteritis nodosa. The presence of this disease is suspected in all instances of pyrexia of unknown origin which is accompanied by leukocytosis and eosinophilia.

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or a cutaneous lesion Thus the correct diagnosis of periarteritis nodosa has been made by histologic study of the appendix or the gallbladder removed at operation when the organ was suspected of being acutely inflamed.

The disease lasts from a few days to several years. It is often fatal.

Rheumatic Fever. Synonymous names for rheumatic fever are acute articular

the cutaneous reactivity is known to have been acquired recently. It is well to recall too that in advanced stages of all infections, including tuberculosis, the skin may fail to react· this condition is called *anergy* and has been considered a consequence of an exhaustion on the part of the tissue cells. Also in intercurrent infection such as measles and chickenpox, even the tuberculous host may temporarily cease to give skin reactions to tuberculin or other test substances. A positive reaction which is specific may not always be of *practical diagnostic value; the interpretation of* positive reactions may be of little or no diagnostic value when all members of a certain segment of the population have been exposed to the infecting agent or to closely allied genera or species which produce similar sensitivity to that of the suspected infecting agent.

The cutaneous and sometimes the patch test are of value in the detection of certain natural and acquired allergies to drugs and other chemical agents. For instance, a patient may be suspected of and found to be sensitive to diodrast. In instances of sensitivity, penicillin and streptomycin may be tested intracutaneously

Any means of testing may give falsely negative reactions in allergies to the sulfonamides

DIAGNOSIS

The diagnosis of allergic state and disease depends on the discovery of the causative agents. The complexities of the diagnostic task are enlarged because there often are many different etiologic agents responsible for the same group of symptoms. Even geographic change may not be of diagnostic importance if in the new environment there are new antigens to which the patient is just as hypersensitive as he was to the old ones The use of skin tests as a means for discovering specific sensitivity has become widespread; yet the etiologic diagnosis is seldom accomplished by the application of these procedures alone Disappointing indeed are the diagnostic implications portrayed by reactions to skin tests indicating a marked sensitivity to a particular allergen, when the patient is known never to have had contact with this substance That the diagnostician who diagnoses allergic disease should be well versed in the sources and contacts of specific substances, their usual as well as unusual occurrences in the environment of the patients, is mandatory

In the diagnosis of disease due to pollen, reference works in botany listing the geographic distribution of proved hay fever-causing plants are helpful. It is understood that when these references are used, approximate distributions and average seasonal dates for the appearance of certain pollens are given These reference works consist of lists of wind-pollinated plants, and the approximate periods of bloom, together with estimates of the amount of distribution.

Pollen counts furnish information concerning atmospheric pollen pollution both qualitative and quantitative The pollens which cause hay fever are so nearly the same that any differences in the antigenic properties of pollen of species of the same taxonomic group cannot be distinguished.

Despite all of the inherent diagnostic difficulties, if it is realized that these difficulties may be present, the history of the illness and the findings on physical examinations correlated with the appropriate selection of specific tests permit of a correct diagnosis in most instances of allergic disease

CHRONIC DISEASE AND ALLERGY

(Collagenous Diseases; Chemical Anaphylaxis)

Rich and others have stimulated anaphylactically sensitive animals repeatedly with large amounts of *antigen* with the intention of producing chronic tissue changes similar to those found in certain human diseases In recent years such changes in the tissues of animals have been produced which resemble those of periarteritis

The cardiac lesions of rheumatic fever are dispersed throughout the endocardium, myocardium, pericardium and conduction system The specific lesions are the Aschoff bodies, which are of microscopic dimensions They occur in association with small blood vessels in the subcutaneous tissues, but most importantly in the subendocardial regions of interstitial tissue of the left ventricle. The pericardium becomes thick and rough, numerous adhesions are formed between the pericardial layers and are adherent to neighboring extracardiac structures Calcification may occur. The lesions of the left atrium consist of raised series of ridges ranging from light gray to light yellow in color. The ridges are situated on the posterior wall immediately above the posterior cusp of the mitral valve When the disease is inactive, the lesions become translucent. In the active stage the valve cusp is thickened, with loss of transparency, and verrucae are present The verrucae appear as rows of fine, clear grayish or yellow vegetations on the closure line of the valve The predilection for the mitral valve is due to the peculiarity of its blood supply.

The atrioventricular chordae and cusps may become shortened With the shortening of the chordae and changes in the auricular endocardium a stenotic valve is formed. Infiltration with lime increases the rigidity and stenosis of such a valve The semilunar valves likewise become thickened and shortened

The occurrence in rheumatic fever of partial heart block may be due to lesions in the conduction system by the rheumatic process

Rheumatic pneumonia, serous pleurisy, and peritonitis are commonly present in acute stages of rheumatic fever

In chorea, cerebral lesions consisting of a meningo-encephalitis and cardiac lesions identical with those present in rheumatic fever may be present in the same person.

Symptoms Rheumatic fever is characterized by its chronicity, variety of forms, and tendency for remissions and relapses of symptoms For instance, the first attack may be one of chorea, the second, polyarthritis and the third, pancarditis The acute attacks generally last 1 to 3 months, but occasionally there are fulminating instances of the disease ending fatally in several days or weeks The acute attack is followed by a period of varying lengths of time in which there may be no symptoms.

The onset may be insidious or acute. Often there is a history of sore throat, tonsillitis or scarlet fever from which an apparent recovery took place Often full *recovery from the infection did not occur and there was a continuing loss of body* weight, epistaxis, and unaccountable weakness, fever and night sweats

Loss of body weight may be extreme Recordings of body weight at regular intervals may prove to be a valuable indicator of the progress of rheumatic fever An increasing body weight during the course of a rheumatic attack often signifies the beginning of convalescence.

Nosebleed is a common symptom of rheumatic fever in children, especially during rheumatic activity or before a recurrence.

In adults *arthritis* is the commonest local manifestation of the disease. In children rheumatic arthritis is not nearly so common as it is in adults In adults there is a symmetric, rapidly developing arthritis, usually limited to the large joints. The inflammatory symptoms subside as rapidly as they developed At times the inflammation seems to involve other joints as inflammation regresses in those previously affected A single joint only may be affected. In both adults and children the large joints are more frequently involved, however, almost any joint may be affected, including the small joints of the hands and feet, the vertebrae, the sternoclavicular, temporomandibular and cricoarytenoid joints and the symphysis pubis.

The respiratory symptoms consist of those referable to a pleurisy, in some instances a low-grade pneumonia

Gastrointestinal and abdominal symptoms consist of constipation, diarrhea and abdominal distention which in children often usher in the first attack or subsequent attacks of rheumatic fever

When abdominal pain arises in the course of a well-developed attack of rheu-

rheumatism, the rheumatic state, acute rheumatism, specific infectious rheumatism, acute rheumatic polyarthritis, rheumatic granulomatosis and Bouillaud's disease.

Rheumatic fever is a chronic inflammation-like disease which affects the joints primarily and the heart secondarily It is characterized by remission and relapses and often by a progression of the cardiac symptoms with each successive relapse The carditis of rheumatic fever places it in a position equal to that of arteriosclerosis as a cause of heart disease The cardiac injury sustained from rheumatic fever may be fully compensated for, and the patient lives comfortably until hyperthyroidism, pregnancy, septicemia, severe anemia or arteriosclerosis begins to affect the heart, it is then that the rheumatic lesions become manifest for the first time.

Often rheumatic fever has been considered to be of infectious nature. Belief in the infectious origin of rheumatic fever is based on the observation that the disease may occur in epidemics, or after infectious disease, has high familial association, and that its seasonal incidence is similar to that of the hemolytic streptococcus. Hemolytic streptococcal infections and rheumatic fever are similar in their geographic, climatic and seasonal incidence

In the practice of medicine it is often observed that sore throat, tonsillitis or scarlet fever (erythrogenic strain) due to the hemolytic streptococcus (Lancefield's type A) just prior to an attack of rheumatic fever is common. These acute streptococcal infections may occur in epidemics which are followed by epidemics of rheumatic fever 1 to 3 weeks later. Familial outbreaks of hemolytic streptococcal infections are followed in some members of the family by suppurative lesions such as otitis, in others by acute glomerulonephritis and in still others by rheumatic fever. Epidemics of pharyngitis and tonsillitis in crowded schools have similarly been followed by an outbreak of rheumatic fever Probably more important is the observation that in young patients a throat infection caused by hemolytic streptococci may be followed by rehumatic fever, or that such an infection may cause an exacerbation of an existing rheumatic state.

Rheumatic fever or rheumatic heart disease has never been proved to be produced by hemolytic streptococci. Results of blood cultures during the active uncomplicated stages of these diseases are negative for hemolytic streptococci.

The belief has been expressed that rheumatic fever is an allergic response to infection with hemolytic streptococci Others are of the opinion that rheumatic fever is an allergic response to any of the streptococci, hemolytic or nonhemolytic, or even to other microorganisms A few have concluded that rheumatic fever may result from sensitization to many types of foreign proteins, bacterial or nonbacterial

Rich produced lesions which he considered typical of rheumatic fever in the hearts of previously sensitized rabbits by the injection of horse serum Because of the evidence that periarteritis nodosa is an "allergic" disease and because Rich found that both periarteritis nodosa and rheumatic fever could be produced by the same technic of foreign protein sensitization, he concluded that rheumatic fever is also an allergic disease with lesions due to anaphylactic hypersensitivity in a sensitized person.

The greatest incidence of rheumatic fever is in January, February, March and April. The disease has a higher incidence in urban and suburban populations than in rural folks. Rheumatic fever can and does affect children who are well fed and clothed. In this respect it is like some of the viral infections.

Nine of every 10 have their first attacks of rheumatic fever before the age of 15 years. More attacks occur between the ages of 5 and 10 years than between 10 and 15 years Less frequently rheumatic fever begins between the ages of 15 and 20 years. Excluding the girls who have chorea, the incidence is essentially the same in both sexes. Likewise the disease has no racial preference.

Acute rheumatic fever affects tissues lined by endothelium, such as the blood vessels, endocardium, pericardium and synovia.

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When abdominal pain arises in the course of a well-developed attack of rheu-

matic fever, it is not likely to be misinterpreted. However, it may precede any definite rheumatic symptoms There may be abdominal tenderness, nausea and vomiting. Abdominal pain most commonly is referred from the thorax when there is pericarditis or pleurisy. There may be polyserositis including perihepatitis as well as pleuropericarditis. In right heart failure, pain, abdominal tenderness and vomiting may be due to a congested liver.

Acute diffuse glomerulonephritis is uncommon. Chronic glomerulonephritis frequently is combined with rheumatic heart disease. The combination is no commoner, however, than is to be anticipated from the incidence of the two diseases, *both frequently* commencing with a throat infection by streptococci

The presence of almost constant fever is the commonest complaint. Often the temperature may rise only to between 100 and 101 F (37 8 and 38 3 C), and at certain times of the day it is normal. When the local symptoms of arthritis or cardiac disease develop, the fever increases and is irregular, but when the local symptoms disappear the low-grade fever returns.

A high fever is rare in rheumatic fever except in rheumatic hyperpyrexia which usually is a terminal event The terminal rise in temperature to 106 to 107 F (about 41 to 41 7 C) occasionally occurs. Rheumatic hyperpyrexia often occurs in the second or third week of the first attack, sometimes when the infection is subsiding and convalescence seems to have begun

Rheumatic hyperpyrexia is associated with symptoms of cerebral rheumatism Delirium at night (when not due to salicylates) and excessive micturition are premonitory symptoms Convulsions, squint, risus sardonicus, opisthotonos, deafness, irregular respiration, lividity and progressive coma may develop Rheumatic hyperpyrexia has been practically eliminated since the introduction of salicylates in the treatment of this disease

The fever is variable in duration. In abortive instances it may be absent except for a few days at a time In definite attacks the fever may last for a few weeks up to a few months. If all symptoms subside except the fever, the disease is still active Occasionally, however, the temperature is normal despite the presence of active infection. In chorea, which is generally accepted as a manifestation of active rheumatic fever, *the temperature may remain normal throughout the attack* In the prearthritic or precardiac stages of rheumatic fever there is often no fever although progressive anemia, fatigability and loss of weight indicate active disease. Similarly there may be no fever toward the end of a rheumatic attack when all symptoms have disappeared; yet there may be persistent rheumatic inflammation as indicated by tachycardia, leukocytosis and increased rate of sedimentation of erythrocytes. There may be little or no fever with subcutaneous nodules although these represent active rheumatic disease

Sweating may be limited to the night or may occur throughout the day and night, and may become severe enough to cause maceration of the skin

In *rheumatic myocarditis* precordial pain of variable severity is frequent. This pain occurs without exertion and may be due to an associated pericarditis or to disease of the coronary arteries It may simulate true angina pectoris Precordial pain is distinguished from precordial distress due to palpitation and tachycardia, which is common.

Examination The findings on examination depend on the stage, the degree of severity and the presenting manifestations of the attack or the attacks

Usually there are observed a loss of body weight, pallor and weakness The pulse is full, bounding, easily compressible and often dicrotic. A tachycardia of 100 to 140, which is out of proportion to the fever, is a common sign of rheumatic activity. In convalescence there may be bradycardia. When the temperature has subsided, a persistent tachycardia with or without fever usually indicates continued rheumatic activity, probably within the heart

The significant cutaneous lesion is variously termed erythema annulare, erythema marginatum, erythema circinatum, or erythema gyratum according to its configuration. These lesions occur on the thorax or on the extremities They begin as reddish macules or papules 1 to 5 mm. in diameter and develop rapidly. As the lesions enlarge their centers become a dull brown in color. The lesions have pale pink or dull red margins, sharply circumscribed and slightly elevated

The subcutaneous nodules are commonest in children but may develop in young adults. The nodules are rounded elevations varying in size from a few millimeters to about 2 cm (4/5 inch) in diameter. They are situated subcutaneously, unattached to skin so that the skin can be moved freely over the nodule They tend to assume a symmetric distribution They occur on the extensor surfaces of the hands or the feet, elbows, on the malleoli, patellae, skull, spines of scapula, vertebrae, clavicles, ribs, crests of the ilium, sternum and acromion, and rarely the flexor tendons of the hand may be involved There is no redness and usually neither pain nor tenderness. The nodules vary in number from a few to many. The characteristic rapid evolution and disappearance of nodules are followed by the appearance of other nodules in another location The successive appearances of these nodules may be observed for weeks or months.

There are disability and pain, redness, swelling and increased warmth of the skin overlying the joint. Synchronous with the onset of arthritis, a rise in fever and an intensification of all other general symptoms ensue. The pain may be so intense as to make the weight of the bedclothes or jarring of the bed intolerable. Swelling is chiefly of the periarticular tissues In the large joints there may be intra-articular effusion with fluctuation. Suppuration does not occur except in the presence of a septicemia of pyogenic organisms which in many instances originate from a focus in the throat Pain in the juxta-articular region may be due to inflammation of neighboring tendons and muscles. Tendon sheaths as well as tendons may become inflamed. In tenosynovitis of the hand considerable effusions may occur. Myalgias are common They are responsible for the "growing pains" in the legs of children.

The clinical signs of endocarditis result essentially from inflammation of the valve ring and cusp. The development of endocarditis is manifested by an alteration in the heart sounds, the occurrence of cardiac murmurs, or a change in the character of murmurs already present.

At the onset of rheumatic endocarditis it will be observed that there is a loss of the distinctive muscular quality of the first sound of the apex. Sometimes a splitting or reduplication of the second sound at the apex will be the only manifestation Early and frequently a blowing systolic murmur, situated at the apex, to the left of the sternum, at the level of the fourth rib, over the pulmonic or aortic area or over an extensive precordial area is heard It is impossible to distinguish the systolic murmur occurring early in active rheumatic fever from functional murmurs. Occasionally a middiastolic murmur appears in the early stages of rheumatic fever and disappears with the rheumatic attack

In the active stage of rheumatic fever an acute fibrinous pericarditis and pericarditis with effusion may occur The onset of a pericarditis is often synchronous with an increase in the fever.

The essential symptom of pericarditis is substernal, precordial or abdominal pain, and the essential sign is a pericardial friction rub. The precordial pain and pericardial rub of the acute fibrinous pericarditis may or may not disappear with the formation of a considerable effusion The patient may suffer from precordial oppression and a sense of anxiety Restlessness, insomnia, delirium and other mental symptoms may occur With large effusions the patient is exceedingly dyspneic and orthopneic so that he must sit upright in bed He may become cyanotic or flushed, but often he presents an intense pallor. Dysphagia, aphonia and an irritative cough may result from pressure on the esophagus or recurrent laryngeal nerve

The earliest signs of myocarditis are changes in the quality, intensity and pitch of the first sound. The first sound becomes enfeebled. The clinical evidence of pericarditis indicates a serious form of rheumatic heart disease. Pericarditis often is associated with pleurisy and pneumonia

Cardiac enlargement may appear rapidly with active rheumatic heart disease if there is severe myocardial infection with failure. It can be interpreted as a sign of rheumatic activity only if there are other evidences of active rheumatic fever. Disturbances of cardiac rhythm are frequent and valuable signs of rheumatic myocarditis. The arrhythmias are often clinically recognizable, discovery and confirmation of their exact nature require electrocardiograms

Evidences of right and left heart failure are commonly observed in children suffering from severe forms of rheumatic myocarditis. Cardiac failure is often seen in adult patients who have inactive rheumatic heart disease and who experience an acute recurrence

Inactive rheumatic heart disease is essentially valvular disease of the heart.

A polymorphonuclear leukocytosis is common in active rheumatic fever and is a *significant index of active infection* The leukocyte count is generally between 10,000 and 20,000 per cubic millimeter of blood. Occasionally it may exceed 20,000 or it may lie within normal limits. A leukocytosis may persist after the fever has gone. It then becomes an index of rheumatic activity Rheumatic activity may persist, however, even after the leukocyte count has fallen to normal There is a shift to the left in the number of nonfilamented polymorphs by the Schilling count The remaining white cells are normal, but in chorea there may be an eosinophilia

Anemia, the cause of the characteristic pallor, is commonly present in active rheumatic fever The hemoglobin may fall as low as 6 or 7 gm. per 100 ml of blood although it usually lies between 8 and 12 gm and gradually rises as active infection subsides The erythrocyte count ranges between 3,000,000 and 4,000,000 per cubic millimeter The anemia is of the microcytic type

Electrocardiographic abnormalities are almost always present at some time during the course of active rheumatic fever Three types of electrocardiographic abnormalities are described by cardiologists (1) impaired atrioventricular conduction, (2) abnormalities in the QRST complex and more rarely in the P wave and (3) changes in cardiac rate and rhythm

Diagnosis The diagnosis of rheumatic fever in the early stages may be only presumptive The disease is most easily diagnosed in retrospect when there is well-developed valvular heart disease

The diagnosis of rheumatic fever and rheumatic heart disease requires the recognition of an active rheumatic fever with or without cardiac involvement, and of rheumatic heart disease in patients who have passed the period of *rheumatic* activity. In the absence of involvement of the joints or the heart the diagnosis can be suspected but not made

Rapid cardiac rates after the temperature is normal often are present when *there is persistent rheumatic activity* Occasionally a rapid pulse rate appears during convalescence if the patient is gradually permitted to resume activity. This appearance may not indicate a persistent rheumatic activity It is the *result of resumption* of physical activity after a long illness However, a fast heart rate attended by a leukocytosis in a convalescent patient usually denotes the presence of *persistent rheumatic activity*.

Distinct prolongation of the PR interval and a prolonged QT interval in the electrocardiogram may help to identify rheumatic heart disease.

Rheumatic fever is to be differentiated from infections of the respiratory tract, rheumatoid *arthritis in adults* and Still's disease in children, subacute bacterial endocarditis, pulmonary tuberculosis, and acute appendicitis when abdominal symptoms are prominent.

Recovery is the rule in the first acute attack of rheumatic fever. If the initial attack is experienced before the age of 10 years, a recurrence is to be anticipated in most of these patients but not in all.

Rheumatic pericarditis is serious both because of relatively high immediate mortality and because of the probability of permanent cardiac damage. The presence of auricular fibrillation in children is serious. In adults auricular fibrillation may persist for years.

The *complications* of rheumatic heart disease are: cardiac failure, auricular fibrillation and other arrhythmias, subacute and acute bacterial endocarditis and embolization

Chorea Minor (Sydenham's Chorea, Saint Vitus' Dance). The essentially rheumatic nature of chorea minor (Sydenham) is no longer doubted, although chorea is not always associated with active rheumatic fever. Chorea is primarily a manifestation of rheumatic fever in childhood It may be the first symptom and is frequently complicated or followed by carditis.

At least one half of the instances of chorea in children are unaccompanied by other symptoms of rheumatic fever or by the development of cardiac disease. These nonrheumatic instances are characterized by absence of family history of rheumatic fever, by absence of preceding respiratory infection, and by normal leukocyte count and sedimentation rate during the attack of chorea

Pathologically chorea (Saint Vitus' dance) is a meningo-encephalitis involving particularly the basal ganglia, especially the caudate nucleus and putamen in the corpus striatum, and also the internal capsule and cortex In pregnancy it is occasionally observed in a severe form (chorea gravidarum); abortion or premature induction of labor may be required

The onset of chorea is usually insidious It may commence after an injury, fright or an emotional upset

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wetting As the disease advances, exaggerated un-co-ordinated and explosive movements occur spontaneously as well as with muscular effort and are beyond voluntary control Facial grimaces, rolling of the eyes, tossing of the head and wrinkling of the forehead combine to form an imbecilic appearance The children soon begin to slur their words and to phonate badly The gait is awkward, and too rapid A hand or half of the body may be affected, simulating hemiplegia The patients may become unable to swallow, and lose control of bladder and bowels. The nature of the disease can be verified by holding the patient's hands enclosed in those of the examiner, whereupon the exaggerated twitchings are observed In all, the movements are constant, un-co-ordinated and purposeless.

The attack of chorea may last 6 to 8 weeks or longer Recurrences, sometimes with additional cardiac damage, may be observed. Death rarely occurs except in pregnant women, of these, 1 or 2 of every 10 who have the disease will die.

Chorea minor is distinguished from choreiform movements of cerebral palsy; from general tic disease, from hysteria (the so-called chorea major or magna is hysterical, in most female patients more than 16 years old choreiform movements are hysterical), from Huntington's chorea (on the basis of age, etiology, heredity, chronicity, and dementia) and from double athetosis

Relapsing Febrile Nodular Nonsuppurative Panniculitis (Weber-Christian Disease). The etiology of relapsing, febrile, nodular, nonsuppurative panniculitis is unknown. This disease is regarded not as a disease entity but rather as an allergic systemic reaction to nonspecific stimuli, with focal manifestations in the subcutaneous or intraperitoneal fat, resulting in destruction of the supporting framework of

the fat cell and liberation of free fat. Nodular panniculitis is probably allied to th group of collagen diseases

The disease occurs more frequently in females than in males in every age group and occurs most commonly as a single entity, unassociated with another specific disease There have been no epidemics.

The nodule consists of fatty tissue which is thicker and denser than normal. Various stages of fatty atrophy in the same piece of tissue may be observed.

The interstices of the adipose tissue are infiltrated with leukocytes, with separation and partial to complete resorption of fat cells Serous atrophy and even necrosis of fat have been observed Eventually the fat cells are completely replaced by scar tissue, which generally contracts to dimple-like skin depressions The liver appears fatty and the spleen is enlarged There are fat emboli in the lungs. The cells of the adrenal cortex show hydropic degeneration

SYMPTOMS. Relapsing, febrile, nodular, nonsuppurative panniculitis is characterized by recurrent episodes of fever, the temperature ranging as high as 104 F (40 C), and by single to multiple recurrences of tender or painless, freely movable nodules ranging from about 0 5 to 3 cm in diameter in the panniculus adiposus. The nodules do not produce pus and may regress in a few days or weeks, either leaving a shallow dimple in the skin or showing no superficial evidence of their site. The overlying skin may be normal in color but usually is red

EXAMINATION The nodules are usually a few centimeters in diameter, are movable beneath the skin, may be tender and firm, and are most commonly found on the thighs, legs, abdomen, breasts and arms Some nodules may attain 20 cm. in diameter or may be even larger They may occur on other parts of the body, including the scalp, neck, hands, and back.

The nodules may remain from several days to months, finally regressing and leaving dimples in the skin or disappearing without any superficial trace Usually there is no suppuration or break in the skin The nodules tend to enlarge during the height of the fever.

The spleen may enlarge slightly. The liver does not increase in size. The regional lymph nodes are enlarged

Recurrences, with the same clinical findings, occur at intervals of a few days, weeks, months or years Patients who had frequent relapses have been followed for years Between relapses the only evidence or residuum of the disease may be the dimpled skin where lesions have regressed.

DIAGNOSIS A biopsy is important in establishing an accurate diagnosis. A diagnosis of relapsing, febrile, nodular, nonsuppurative panniculitis is made on the basis of clinical course, the typical subcutaneous nodules and the histopathologic findings of the nodules The disease is suspected from its clinical course and findings on physical examination.

Lupus Erythematosus. Lupus erythematosus appears in many varieties and forms. It may be acute or subacute but more commonly it is chronic. The subacute and chronic forms are characterized by cutaneous lesions These lesions are rather ill-defined patches which are mostly circular, varying in size, covered with oily appearing desquamating rough skin, laterally limited by fine scarring as the lesion spreads. When the scabs are removed, small projections may be revealed on their lower surfaces which have extended into the skin follicles. The lesions usually begin on the face, ears, and scalp, and over the upper part of the sternum, back and hands Affecting simultaneously the bridge of the nose and the cheeks, they produce a butterfly configuration.

... scaling irregular

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ay be involved.

The lesions may remain stationary in size for years. Some patients seem to recover from this form of lupus erythematosus.

Disseminated Lupus Erythematosus. Disseminated lupus erythematosus is a prolonged febrile disease usually accompanied by cutaneous manifestations, and may resemble rheumatic fever, rheumatoid arthritis, chronic nephritis, or Libman-Sacks disease. In some instances the cutaneous manifestations may be absent. The disseminated form of the disease is fatal, after a variable period which may be weeks, months or years

The etiology is unknown. The disease has many features resembling other conditions, which often are termed collagen diseases. Recent investigators have rejected the concept of tuberculous origin of the disease. Disseminated lupus erythematosus most commonly affects young women.

PATHOLOGY. There are widespread structural alterations of the connective tissue. These changes affect the heart, kidneys, serous membranes, blood vessels, lymph nodes, muscles, skin, and mediastinal and retroperitoneal tissues. There is a specific predilection for the heart, glomeruli, blood vessels, skin, spleen and retroperitoneal tissues In biopsies of 96 cutaneous lesions of disseminated lupus erythematosus, Montgomery and McCreight found alterations of collagen in less than one fourth of their cases of chronic, subacute and acute disseminated lupus erythematosus. In most instances in which fibrinoid degeneration could be demonstrated, it was minimal and no greater than that seen in many other chronic inflammatory infectious diseases of the skin.

Hargraves, Richmond and Morton observed in preparations of bone marrow in only certain cases of acute disseminated lupus erythematosus a cell termed by them the L E cell This cell is a mature neutrophilic, polymorphonuclear leukocyte which differs from other similar cells by the structure of the engulfed material In the L E cell the engulfed mass, characterized by lack of chromatin structure, is almost homogeneous and has a smoky appearance

Montgomery and McCreight were able to demonstrate the lupus erythematosus cells described by Hargraves in sternal aspirations in 5 of 7 cases of acute disseminated lupus erythematosus and in 3 of 18 cases of subacute disseminated lupus erythematosus These cells have not thus far been observed in any other condition, except in 1 case of myeloma They may provide an important diagnostic feature of the disease.

Montgomery and McCreight maintained O'Leary's classification of chronic, subacute and acute types of lupus erythematosus The chronic type has also been termed the generalized discoid type. Sensitivity to light in acute disseminated instances, lesions of the mucous membranes, fever, the presence of infected tonsils, leukopenia, false positive serologic reactions and renal disorders all occur Any organ may become involved, although the tendency has been to focus attention on cardiac, renal, hepatic, splenic or arthritic involvement. It is emphasized that there are also ocular and gastrointestinal symptoms

SYMPTOMS The symptoms of lupus erythematosus are varied They cannot be enumerated except as they occur in association with the organ or organs affected In the active stage there is constant fever and there may be arthralgias, weakness, loss of weight, fatigue, characteristic erythematous eruptions, ulcerative lesions of the mucous membrane of the mouth and local or generalized lymphadenopathy. There may be clinical evidence of pneumonia Often the manifestations are those of a glomerulonephritis with albumin and erythrocytes in the urine A retinopathy may be present. It is now known that *Libman-Sacks disease* characterized by atypical verrucous nonbacterial endocarditis is a manifestation of lupus erythematosus.

Tumulty and Harvey emphasized the importance of manifestations due to involvement of the nervous system In their series of 32 patients, 4 had convulsive episodes, 4 presented toxic psychosis, 3 patients had transient periods of coma, 3 had hemiplegia, 2 had transient episodes of bilateral ptosis and 1 had attacks of jacksonian epilepsy.

Baehr and Pollack stressed that the predominant occurrence of lupus in skin exposed to sunlight and wind is not the primary manifestation of lupus erythematosus, and that these lesions are not responsible for the alterations in the viscera. The cutaneous lesions may be absent throughout the entire course of the disease or may appear only during acute exacerbations or in the terminal stage.

EXAMINATION. The findings on physical examination are exceedingly varied and complex, depending on the organ or organs involved

The cutaneous lesions of the disseminated form of lupus erythematosus may develop at any time during the course of the disease. They consist of slightly raised erythematous butterfly eruptions across the bridge of the nose and extending to the cheeks Papular and erythematous lesions of a bluish red cast affect other parts of the face, the forehead, the ears, the manubrium sterni, the volar surface of the fingers, the thenar and hypothenar eminences and other parts of the upper and lower extremities Telangiectatic and petechial lesions occur over the extremities The skin of the face may become scaly and edematous, and the lesion may resemble that of seborrheic dermatitis or erysipelas Erythematous or ulcerative lesions may appear over the face, lips and on the hard palate or other parts of the oral mucosa Healing of these lesions may leave ugly scars.

The liver and the spleen may be palpable. The lymph nodes are often enlarged

Albuminuria and microscopic hematuria often are present The fundi may contain cotton-wool exudates and hemorrhages due to local vascular lesions Fleeting or persistent pleurisy with effusion which may be eosinophilic often is present. Evidence of serofibrinous pericarditis is commonly observed. Raynaud-like phenomena, scleroderma, cerebral manifestations, evidences of impaired renal functional activity, bronchopneumonia and bacterial endocarditis appear late if at all in this disease Leukopenia, anemia, occasional thrombocytopenia, a reduction in plasma albumin, hyperglobulinemia and an occasional false positive serologic reaction are sometimes present

The albumin-globulin ratio may become reversed as the disease progresses. Aspiration of sternal marrow will reveal lupus erythematosus cells, as described by Hargraves and associates in the disseminate type when the disease is active or is increasing, but these cells are not demonstrable when the condition is quiescent.

DIAGNOSIS The combination of fever, arthralgia, lupus erythematosus and leukopenia is usually diagnostically suggestive In the absence of characteristic cutaneous lesions the presence of lupus erythematosus may not be suspected, and then the diagnosis will be that of the dominant manifestation.

In the absence of characteristic cutaneous lesions, acute lupus erythematosus may be suspected in illnesses resembling rheumatic fever in which there is evidence of acute glomerulonephritis and hyperazotemia, but with a normal blood pressure. Similarly the association of thrombocytopenic purpura or of leukopenia or both in disease resembling rheumatic fever suggests lupus erythematosus. The combination of hyperazotemia, fever and normal blood pressure may also be due to this disease. Lupus erythematosus may resemble a subacute polyserositis with fever, with or without arthritis and glomerulonephritis This disease may resemble bacterial endocarditis However, blood cultures are persistently negative.

The presence of Hargraves' L E cells, if identification of the cells is made by an examiner of adequate experience, is of diagnostic value. These cells are obtained by sternal aspiration. Hargraves has more recently devised a clot test which is of diagnostic value.

Dermatomyositis. Dermatomyositis is characterized by a subacute or chronic inflammatory-like process involving the muscles, skin and subcutaneous tissues. It may occur at any age of life. The etiology is unknown. It is collagenous in origin.

The skin may be atrophied, and the subcutaneous fat is partially replaced by connective tissue. The blood vessels beneath the skin are thickened or partially occluded. The

muscles are pale, and may be soft and friable, or fibrous, depending on the age of the process. The superficial portions of the muscle which lie directly under the skin are most severely affected.

SYMPTOMS The symptoms commence with pain and swelling and tenderness over the proximal muscles of the extremities The process soon becomes symmetric and general Evidences of infection are almost always present in the early stages of the disease. The temperature may be only slightly elevated or may reach 99 to 100 F (37.2 to 37 8 C). Tachycardia is often present and seems to be independent of the fever. Sweating is profuse and characteristic. Delirium is rare

EXAMINATION. The cutaneous lesions may precede or follow the myositis. There is edema of the subcutaneous tissue or a dense infiltration either with or without redness. The skin of the forehead and the eyelids is involved and gives rise to the characteristic "marble brow" A thickening of the skin and fibrosis of the subcutaneous tissue may be of a degree which closely resembles scleroderma. The cutaneous lesions are likely to appear during the course of the disease and may desquamate. Cutaneous lesions may be entirely absent

The skeletal muscles are at first swollen and edematous. Later they are hypotonic and small In the active stages of the disease there is almost always tenderness on pressure over the involved muscles, and both active and passive movements cause pain Either paralysis or mild paresis may be present Tendon reflexes are normal, diminished or abolished Passive movements reveal loss of the normal elasticity of the muscles In some cases the process may involve the muscles of respiration, giving rise to dyspnea Involvement of the myocardium or myocarditis may cause decompensation which ends in death The jaw muscles may be affected, and the patient becomes unable to chew Tenosynovitis is almost always present to some degree, and in rare cases the joints are affected An extension of the inflammation to the nerve trunks initiates a neuromyositis A neuromyositis is but an extension of a dermatomyositis to the nerve trunks It is distinguished from dermatomyositis by observing that the nerve trunks are tender and sensory disturbances are present.

Severe residua may be found after the active stage of the disease. The muscles may be atrophic and partially replaced by connective tissue so that they feel dense and inelastic. Severe flexor contractures are common The skin is often deeply pigmented and indurated so as to resemble scleroderma Roentgenograms of the muscles sometimes reveal fine calcareous deposits lying in the superficial layers of the muscle, muscle sheath and subcutaneous tissues.

The spleen and lymph nodes may be enlarged There is rarely leukocytosis. A relative eosinophilia often is present.

DIAGNOSIS The diagnosis is established by biopsy The diagnostic features of importance are the tenderness of the muscles, the edema of the subcutaneous tissues, and the dermatitis

The prognosis is unfavorable but not absolutely bad In some cases in which the symptoms are mild the patient may make a complete recovery

Scleroderma (Acroscleroderma, Acrosclerosis, Diffuse Scleroderma). Scleroderma is a disease of the skin and subcutaneous tissues in which there is a hard, rigid, hidebound appearing skin in which often appear pigmented patches When scleroderma appears on small areas of the skin it is designated scleroderma circumscriptum The term acroscleroderma designates mature scleroderma which attends Raynaud's disease

The etiology of scleroderma is a mystery The disease commonly affects young women

PATHOLOGY. In acroscleroderma according to O'Leary and Waisman the cutaneous changes consist of increase and swelling of collagenous connective tissue with fragmentation and swelling of the elastic fibers and an accumulation of melanin in the basal cells The epidermis may be hyperkeratotic, and the rete, the hair follicles and sebaceous

glands are atrophic or absent. In some instances the skeletal muscles undergo changes.

Fibrous tissue changes may be present in the lungs, esophagus, heart and other organs

The esophageal changes in scleroderma consist of dilatation of the distal two thirds of the esophagus and chronic ulceration in the region of the phrenic ampulla In the later stages stricture is present.

SYMPTOMS. The symptoms of scleroderma depend on the situation and distribution of the process Scleroderma attending Raynaud's phenomenon, situated in the upper extremities and termed acroscleroderma, commences in about one half of these patients with aching, soreness, stiffness and swelling of the joints and of the fingers and toes *In about a fourth of patients the first symptoms are coldness,* increased sweating, and cyanosis made worse by being cold. In the rest of the patients articular and vascular symptoms are so intermingled that it is impossible to distinguish the one from the other.

In the syndrome of acroscleroderma the manifestations of Raynaud's phenomenon are far advanced and in these patients the scleroderma involves not only the extremities but extends to the skin of the face and upper thorax. However, the *syndrome of acroscleroderma may involve the skin of the extremities, face and* thorax with minimal manifestations of Raynaud's phenomenon. Finally there are patients who have stiffness of the skin attended by progressive sclerodermatous changes without any subjective or objective evidence of vascular disease including Raynaud's phenomenon.

Sclerodactylia is the term employed to designate the condition when the process and the symptoms are confined to the fingers. When the process is thus limited the *symptoms may closely resemble rheumatoid arthritis.*

The symptoms of scleroderma commence gradually and are manifested by tensing and stiffening of the skin This discomfort is experienced only during use of the fingers in performance of co-ordinated movements As Raynaud's phenomenon progresses, the symptoms are manifested in warmer environments In the early stages the vascular or sclerodermatous changes rarely involve the feet With progression the sclerosis of the skin and subcutaneous tissues eventually involves the *toes, feet and legs, and in the more severely progressive instances the entire surface* of the body including the mucous membranes is affected. As the skin or the mucous membrane becomes involved the patient complains of sensations of stiffness therein

The patient may complain of dysphagia The constricting effect of scleroderma of the thoracic wall, changes in the larynx, and pulmonary fibrosis eventually produce considerable respiratory difficulty Pleural effusion, pericardial effusion and heart failure as the result of scleroderma have been recorded In rare instances, in *the midst of the disease, hydrarthrosis may supervene.*

EXAMINATION Sclerodermatous skin is tight but not necessarily thickened It may be difficult to wrinkle it by pinching The underlying tissue is stiff and hard. In the late stages the fingers become stiff, puffy and fixed and the hands may have a clawlike appearance. The pulsation of peripheral arteries is often *variable and* may be difficult to palpate on account of rigidity of the tissues.

Disturbances of skin pigments are present Hyperpigmentation and depigmentation of the skin may result in the presence of brown pigmentation and vitiligo in the same region The subcutaneous tissues become thinner and atrophic The nails become deformed, shrunken, cracked and lusterless. Gangrene of the end of a finger or toe may appear. The distal ends of the bones of the fingers may become fragmented and may form *sequestra with resulting draining sinuses.*

The roentgenologic examination of the esophagus may reveal loss of peristalsis and dilatation of the distal segment with ulceration. As the disease advances ulceration and stricture may be demonstrated.

In the more advanced stages there may be pulmonary fibrosis and cardiac enlargement

DIAGNOSIS. No other disease produces the hard, tight skin over the fingers, hands and arms, and the expressionless face, thin lips and difficulty in fully opening the mouth as does scleroderma

In most instances of Raynaud's disease the sclerodermatous changes are absent or appear only late in the disease. However, in some instances sclerodermatous changes precede the Raynaud's phenomenon. In rare instances scleroderma proceeds without vascular changes.

Occasionally rapidly progressive scleroderma simulates dermatomyositis and lupus erythematosus. In dermatomyositis the changes are deeper and involve largely the muscle and its fibrous sheath. In lupus erythematosus the skin does not undergo changes in tension and appearance such as occur in scleroderma.

According to O'Leary, Waisman and Harrison scleroderma of the acrosclerotic type reaches a stage where it may remain more or less stationary, but usually it is progressive

Sarcoidosis. Sarcoidosis is called also Boeck's sarcoid, Besnier-Boeck disease, Besnier-Boeck-Schaumann disease, Hutchinson-Boeck disease, lymphogranulomatosis benigna, Darier's sarcoid, erythema induratum, lupus pernio, tuberculosis nodularis, angiolipoid, uveoparotid fever, and osteitis tuberculosa multiplex cystoides.

Boeck's sarcoid is a generalized disease often associated with obscure pathologic processes such as cystic formations in small bones and the syndrome of uveoparotid fever The disease affects the reticuloendothelial system in the lymph structures, spleen, liver, skin and bones The lungs, cardiac muscle, salivary glands and nervous tissue also may be affected. Sarcoidosis is considered by some to be a benign lymphogranulomatosis, by others, a noncaseating form of tuberculosis. Outstanding features of sarcoidosis are an absence or a paucity of tissue caseation, an absence of acid-fast organisms unless frank tuberculosis coexists, and anergy to tuberculin The lesions show a marked tendency to regress The course often is benign, but not always so Death is usually caused by progressive pulmonary tuberculosis or cardiac failure.

Sarcoidosis according to Longcope is neither a new nor a rare disease. The sexes and the races are equally susceptible. Those from rural districts are more frequently affected than urban dwellers, and the disease does occur in more than one member of a family Many authorities believe that it is an infection or that it is related to an infection in some such relationship as rheumatic fever to streptococcus type A infections

In the presence of sarcoidosis active tuberculosis frequently develops, and because of this many have believed that sarcoidosis is an atypical form of tuberculosis

Sarcoidosis bears some clinical similarities to Hodgkin's disease, though histologically it is distinct from it

There are points of similarity to lymphopathia venereum Lymphopathia venereum can be ruled out, however, by the preponderance of negative reactions to the Frei skin test and the failure to isolate this or any other virus from sarcoid either by culture or by animal inoculation

Syphilis, though bearing many resemblances to sarcoid, has been excluded by the usual examinations, including therapeutic tests. There has been no evidence to support the view that sarcoidosis is due to brucella infection.

PATHOLOGY. The sarcoid lesions may occur in all organs of the body but usually are limited to one or two organs or systems. The tissues most frequently involved are the lymph nodes, lungs, eyes, skin, spleen and liver. The cut surface of sarcoid tissue has a

homogeneous appearance, firm, or soft, but never caseous or purulent The lesions vary in size. In some instances there are small nodules in the iris or on an eyelid, or in a lymph node with only slight enlargement of that node. At times the lesions form masses of lymph nodes, cause great enlargement of the spleen, or infiltrate densely throughout the lungs

The lungs in sarcoidosis are large and emphysematous; the visceral pleura is thickened On section, there is a generalized dissemination of millimeter-sized grayish spots as well as larger nodules and patches similar in structure Emphysematous blebs are often present on the surface and small bullae within the lung substance The hilar lymph nodes may reach considerable size

SYMPTOMS. The complaints of a patient who has sarcoidosis depend on the organs involved It is only when a vital organ is involved that there is anything more than a minor discomfort The discomfort in no way indicates the widespread distribution of the lesions. In spite of the number of lesions the patient seems well and has suffered no great loss of body weight If there has been any fever it has not exceeded 101 to 102 F (38 3 to 38 8 C)

EXAMINATION The skin lesions are the commonest and usually the only complaint of the patient These lesions are nodular in type. The nodules are firm and situated deep in the skin and present a semitranslucent, slick or sometimes scaly appearance The lesions are sparsely scattered over all parts of the body The nodules show progression and regression, depending on the progress of the disease, they often have been observed to disappear completely

Enlargement of the lymph nodes may be limited to the hilar nodes or may involve the superficial lymph nodes In the superficial enlargements only a few nodes may be affected or there may be general enlargement.

Lesions of bone may be present in the small bones of the hands and feet. When there are large sarcoid nodules in the hands, there is an irregular enlargement of the phalanges with disability and deformities

Ocular lesions occur in one half of all of those who have the disease Ocular lesions, however, are more regularly associated with thoracic involvement than with involvement of other organs Some patients have enlargement of the lacrimal glands, some have nodules on the lids; often the whole uveal tract is involved with nodules and generalized uveitis Nodules in the iris are irregular in outline, and are larger and more vascular than those due to tuberculosis Ophthalmologists see these lesions best with slit lamp illumination The nodules are situated in the stroma toward both the ciliary and the pupillary borders The first diagnostic suggestion of sarcoidosis comes from the ophthalmologist in some instances.

Sarcoid infiltration may cause nasal obstruction which in appearance resembles carcinoma. A biopsy of this tissue is the only means of diagnosis

An enlargement of one or both parotid glands, involvement of the uveal tract, lacrimal glands and facial nerve with transitory peripheral facial paralysis may be associated with fever (uveoparotid fever). The syndrome of uveoparotid fever has been declared to be characteristic of sarcoidosis

In uveoparotid fever transitory facial nerve paralysis is common. When the central nervous system is involved, the signs and symptoms are unpredictable. [illegible] urine, upper motor neuron lesions, chronic meningo-encephalitis, compression of the [illegible] convulsions and transitory hemiplegia have been recorded as being caused by sarcoidosis

Sarcoidosis frequently involves the hilar lymph nodes without giving clinical symptoms and often without giving findings on examination by physical means. Extensive involvement of the lungs may be revealed by roentgenologic examination A roentgenogram of the thorax is made of every patient who has sarcoid lesions anywhere. Cutaneous, lymph-node, and nasal lesions are the expected findings. There is a tendency for pulmonary lesions to show improvement

The heart and pericardium may be involved and enlarged in widespread sarcoid lesions. The cardiac muscle may be deeply invaded and bundle-branch blocks may be present

The liver may be moderately enlarged and hepatic functional activity may be impaired Jaundice is rarely present. The spleen often is palpable.

Invasion of the pituitary gland with resultant diabetes insipidus, Simmonds' disease, renal lesions and lesions in the muscles has been recorded

Eosinophilia is more likely to be absent than to be present. Tuberculin tests will eliminate tuberculosis if tuberculin anergy is not present. Skin tests for histoplasmosis may be necessary when the lungs are involved

In sarcoidosis usually there is an increased concentration of serum protein, the increment being due to serum globulin of the gamma fraction

DIAGNOSIS The diagnosis depends on the microscopic study of cutaneous nodules or affected lymph nodes In those who have a uveitis the ophthalomogists may make the diagnosis. It is not an easy task for the pathologist to distinguish the hard tubercle of sarcoidosis from the lesions due to true tuberculosis. The tuberculin skin reaction is usually negative in sarcoidosis The roentgenographic appearances of the process in the lungs and bones are distinctive enough to be of value in the differential diagnosis. Active tuberculosis may of course complicate the making of a diagnosis

Sarcoidosis uncomplicated by tuberculosis runs a long course with remissions and exacerbations ending after years in recovery In some instances the uveitis may result in permanent loss of vision Active tuberculosis is prone to develop and to pursue its usual course

Specific treatment is not known, but it would seem best to institute the general hygienic measures which are employed in treatment for tuberculosis.

Amyloidosis. Amyloid is an insoluble protein substance present as an abnormal deposit in the various organs of the body It is homogeneous, translucent and colorless, and is apparently a compound of albumin and chondroitin-sulfuric acid It gives a blue color when treated with iodine and retains Congo red dye

The term lardaceous disease formerly was applied to this condition The disease amyloidosis occurs in both a primary and a secondary form

Primary Amyloidosis. Primary amyloidosis is an unusual disease Dahlin enumerated the differences of primary amyloidosis from the commoner secondary amyloidosis as follows (1) absence of the generally considered specific etiologic factors such as tuberculosis or chronic suppuration, (2) often minimal involvement of the liver, spleen, kidneys and adrenal glands, which are ordinarily the sites of maximal deposition in secondary amyloidosis, (3) usually considerable deposition of the substance in the heart, lungs, skin, striate muscles and other tissues not often involved in the secondary type, (4) often atypical reactions to the specific amyloid stains and (5) the occasional occurrence of amyloid tumors

The etiology is entirely unknown The lardaceous deposits are found diffusely distributed in mesodermal structures It is therefore classed with the collagenous diseases

In the liver the lardaceous deposits are closely applied to the reticulum fibers between the sinusoids and the cords of hepatic cells The same site of deposition is observed in the adrenal gland In the heart the amyloid is situated on the reticulum between the [illegible] blood vessels of [illegible] where it encases [illegible] gastrointestinal [illegible] othelial cells of [illegible] d gland and the pancreas the material appears to be in the connective tissue The adipose connective tissue near the adrenals in some instances shows the amyloid to be deposited on the surface of fat cells, giving their walls a thickened appearance

homogeneous appearance, firm, or soft, but never caseous or purulent. The lesions vary in size. In some instances there are small nodules in the iris or on an eyelid, or in a lymph node with only slight enlargement of that node At times the lesions form masses of lymph nodes, cause great enlargement of the spleen, or infiltrate densely throughout the lungs

The lungs in sarcoidosis are large and emphysematous, the visceral pleura is thickened On section, there is a generalized dissemination of millimeter-sized grayish spots as well as larger nodules and patches similar in structure Emphysematous blebs are often present on the surface and small bullae within the lung substance. The hilar lymph nodes may reach considerable size

SYMPTOMS. The complaints of a patient who has sarcoidosis depend on the organs involved It is only when a vital organ is involved that there is anything more than a minor discomfort The discomfort in no way indicates the widespread distribution of the lesions. In spite of the number of lesions the patient seems well and has suffered no great loss of body weight. If there has been any fever it has not exceeded 101 to 102 F (38 3 to 38.8 C)

EXAMINATION The skin lesions are the commonest and usually the only complaint of the patient. These lesions are nodular in type. The nodules are firm and situated deep in the skin and present a semitranslucent, slick or sometimes scaly appearance. The lesions are sparsely scattered over all parts of the body. The nodules show progression and regression, depending on the progress of the disease; they often have been observed to disappear completely

Enlargement of the lymph nodes may be limited to the hilar nodes or may involve the superficial lymph nodes In the superficial enlargements only a few nodes may be affected or there may be general enlargement

Lesions of bone may be present in the small bones of the hands and feet When there are large sarcoid nodules in the hands, there is an irregular enlargement of the phalanges with disability and deformities.

Ocular lesions occur in one half of all of those who have the disease Ocular lesions, however, are more regularly associated with thoracic involvement than with involvement of other organs Some patients have enlargement of the lacrimal glands, some have nodules on the lids, often the whole uveal tract is involved with nodules and generalized uveitis Nodules in the iris are irregular in outline, and are larger and more vascular than those due to tuberculosis Ophthalmologists see these lesions best with slit lamp illumination The nodules are situated in the stroma toward both the ciliary and the pupillary borders The first diagnostic suggestion of sarcoidosis comes from the ophthalmologist in some instances

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In uveoparotid fever transitory facial nerve paralysis is common When the central nervous system is involved, the signs and symptoms are unpredictable. Argyll Robertson pupils, incontinence of urine, upper motor neuron lesions, chronic arachnoiditis, internal hydrocephalus, meningo-encephalitis, compression of the spinal cord resulting in paraplegia, and convulsions and transitory hemiplegia have been recorded as being caused by sarcoidosis

Sarcoidosis frequently involves the hilar lymph nodes without giving clinical symptoms and often without giving findings on examination by physical means. Extensive involvement of the lungs may be revealed by roentgenologic examination. A roentgenogram of the thorax is made of every patient who has sarcoid lesions anywhere. Cutaneous, lymph-node, and nasal lesions are the expected findings There is a tendency for pulmonary lesions to show improvement.

ripheral nerves where there is extensive degeneration than elsewhere Amyloidosis of the nervous system cannot be clinically diagnosed

Secondary Amyloidosis. Secondary amyloidosis follows long, wasting illnesses, often a suppurative process such as an old osteomyelitis, tuberculosis, actinomycosis, syphilis or protracted intoxication such as a chronic nephritis, cancer or myeloma.

In the secondary form of amyloidosis the spleen, kidneys, adrenal glands and liver are the organs most frequently involved.

The clinical signs and symptoms of amyloidosis in the secondary form of the disease are usually those due to involvement of the kidneys. The kidneys manifest amyloidosis by the signs and symptoms of nephrosis (see Diseases of the Kidneys, Chapter 11). In an occasional instance of the disease, hepatomegaly due to infiltration of the liver with amyloid may be present Even when no hepatic enlargement is present, minimal signs of hepatic failure, apparently the result of amyloidosis, may be present.

Adrenal cortical insufficiency may be present in amyloidosis of the adrenals

Amyloidosis of the intestine may be present without manifest symptoms of disturbed intestinal functions If symptoms should be present, the patient complains of diarrhea

In lipoid nephrosis from 40 to 60 per cent of the Congo red disappears from the blood in an hour However, if the urine reveals the presence ot the dye with the disappearance of more than 40 per cent in the blood, nephrosis is a probable diagnosis

Amyloid and Myeloma Those who have myeloma are prone to the development of deposits of amyloid The distribution of this peculiar material in myeloma is often similar to that observed in primary systemic amyloidosis. Deposits of amyloid may occur within the nodular proliferations of the myeloma cells themselves.

Dahlin and Dockerty expressed the belief that the appearance of amyloid deposition is so characteristic in a myeloma that when amyloid is recognized, an underlying myeloma should be sought if it is not immediately obvious. Similar deposits of amyloid rarely, if ever, occur within other neoplasms The nature of material suspected of being amyloid must be confirmed by the use of special staining reactions The variability of the affinity for Congo red by the amyloid in myeloma is pointed out by Dahlin and Dockerty The van Gieson connective tissue stain is of great value in differentiating amyloid from dense collagen or bone, which stains a brilliant red

DIAGNOSIS OF AMYLOIDOSIS The diagnosis of amyloidosis in the primary form depends on the awareness that the first symptoms in many cases are edema, breathlessness and nocturnal dyspnea Precordial pain may be present Often there is just breathlessness In some there are muscular weakness and limitation of motion of the muscles Difficulty in walking from muscular stiffness may be marked.

A primary amyloidosis may be solely manifested as hepatic insufficiency.

The diagnosis of the secondary form of amyloidosis depends on an awareness that this form of the disease frequently follows a chronic suppurative process present anywhere in the body It is usually manifested as a chronic nephrosis

The diagnosis can be established with certainty by means of histologic examination after the tissue has been stained by a special stain (iodine, methyl violet or Congo red) In accessible areas biopsy is made and the tissue studied by special staining methods

The primary form of amyloidosis is always fatal. The secondary form of the disease may in rare instances become quiescent

Primary amyloidosis appears about equally in the sexes, but, unlike secondary amyloidosis, it occurs more frequently in older patients than in young persons A pronounced asthenia is common Because of the frequently diffuse extent and the varying degree of amyloid deposit in the different organs the myocardium and the lungs may be heavily infiltrated. There may be the symptoms of congestive heart failure In other instances the clinical manifestations are referable to hepatic failure due to the deposits in the liver The association of signs of hepatic disease and renal disease in some may be an outstanding feature. In well-developed renal amyloidosis the manifestations may be those of a nephrosis. A rather rapidly progressive and fatal termination is frequent in a renal amyloidosis being manifested as a nephrosis

In about one third of these patients a loss of body weight is present In others there is a gain of body weight due to subcutaneous edema In some patients there are hydrothorax and ascites

The heart is not enlarged until congestive failure is present. As heart failure develops there may be murmurs, pulsus alternans and gallop rhythms. The electrocardiogram is helpful in detecting, if present, occult cardiac infarction In amyloidosis of the heart there is a low voltage of the QRS complexes.

The liver and the spleen are often palpable

In all forms of primary amyloidosis macroglossia may be present. It is observed in about one third of those who have the disease Dysarthria and discomfort from swallowing are common

Cutaneous changes consist of areas which are opalescent, papular, nodular or diffusely eczematous in appearance When large areas of skin are involved, these changes may be sclerodermatous in appearance. Focal cutaneous lesions of the above-mentioned varieties often occur about the nails of the fingers and toes. Lesions comparable to those of the skin may appear on a thickened enlarged tongue or on the mucous membranes of the throat.

Hypochromic or normocytic anemia is usual The sedimentation reaction is moderately or greatly increased and the leukocytes are normal

The Congo red test is useful The procedure consists in the parenteral administration of 1 ml. of a 1 per cent aqueous solution of Congo red per 10 pounds of body weight In normal persons less than 40 per cent of the dye disappears from the blood in 1 hour In amyloidosis the disappearance of 60 to 100 per cent in 4 minutes is a consistent finding Since small amounts of amyloid may not absorb more than 40 per cent of the dye in 1 hour, the absorption of 40 per cent or less does not exclude amyloidosis The results of the Congo red test may be misleading in individual cases.

The cause of death is renal or cardiac failure, terminal infection and gastrointestinal hemorrhage

Amyloid Neuritis Kernohan and Woltman have observed the infrequency of amyloidosis of the nervous system. Damage to the nervous system, when caused by amyloid, seems to be the result of compression or of arterial obliteration In a few instances the brain may be invaded It is well to remember that corpora amylacea and amyloid are unrelated substances. Small amounts of amyloid have been described in the large vessels of the base of the brain and their branches It is still rarer to observe involvement of the peripheral nerves.

When involvement of the nervous system occurs, it is a part of the general primary or nonseptic form of amyloidosis. As has been noted, the disease process in this form is limited to the media of the smaller arteries and arterioles The amyloidosis of these blood vessels may produce narrowing of the lumina of the vessels or may occlude them The changes in the parenchyma of organs is the result of ischemia subsequent to the narrowing or occlusion of the blood vessels by the amyloid. The results of the ischemia are more specifically observed in the pe-

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19

DISEASES DUE TO TRAUMA, PHYSICAL AGENTS AND CHEMICAL AGENTS

TRAUMA

The term trauma as employed here indicates an agent which, when violently applied, is capable of immediate infliction of a rupture of the continuity of an internal or an external organ or a surface of the body. A gross wound ensues

Classification of Wounds. An *abrasion* is a skin wound caused by scraping or scratching or wearing away of the skin

When an abrasion is inflicted by sliding on the ground or pavement, the direction of the slide is revealed by the angle at which the skin strikes the ground on the starting edge of the injury and tags of skin along the finishing edge Changes in the direction of the body are indicated by curving of the lines of the scratches. Abrasions also may be caused by direct impact by a blunt object Abrasions from falls often affect parts of the body which are made prominent by bony elevations such as the knee or the elbow

A *bruise* or *contusion* is an injury from a blow without an ensuing laceration It causes a spreading extravasation of blood into the tissues from an area crushed by the blow. The skin may be injured by the direct impact. A blow or a fall may leave the skin intact but beneath it the tissues have been crushed sufficiently to tear the capillaries and smaller blood vessels Blood escaping from these will spread and the area will become discolored purple These discolorations are the characteristic manifestations of a bruise

Bruising is manifested more easily in soft, vascular, lax tissues like the eyelids than in tough and less vascular ones like the palm of the hand The young and the old bruise more easily than do persons of other ages

The length of time required for the color changes and the other manifestations of bruises to resolve varies according to their situation Bruises, for instance, seldom resolve when situated under the dura and are slow to resolve in the aged, while those around the eyes or on the scalp resolve in a few days.

A bruise discoloration may shift its position For instance, a deep bruise in the fasciae of the hip may finally discolor the skin at the knee.

A bruise can be caused after death as long as fluid blood is present in the capillaries and veins. The amount of blood escaping in this way can only be very small.

A *laceration* originates from splitting or tearing of the whole skin and is likely to be attended by either abrasions or bruises The extra force which splits the skin is aided by the projection and partial fixation of skin over bony prominences, as with the scalp, cheek, nose, elbows or knees. The edges of such splits are likely to be jagged.

A wound by *incision* is made by a cutting instrument, and incisions vary according to the character of the cutting instrument and the sort of stroke made. A blow with an axe effects a wound with straight but torn edges, whereas a sharp knife or razor inflicts a split-edged wound.

Incised wounds are common in accidents involving broken glass, in accidents

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The *exit wound* consists of a hole in the skin—torn to a degree dependent on the momentum of the bullet leaving the body, and on whether or not it leaves the body straightway, wobbling, or turning over and over, and the amount of bone splinter it may carry away with it. At close range the entry wound is larger than the exit wound.

The course of the projectile is traced by a line commencing at the entry wound and running into the body along the track of the bullet As soon as the bullet meets dense tissue, such as bone or teeth, capable of deflecting it, the jacket may be torn off in the impact, and it with the other solid material may be dispersed in different directions.

A bullet passing through the plates of the skull leaves a hole the margin of which is shelved or beveled from the outside toward the inside of the skull plate. The exit of a bullet from the skull causes a hole in the skull plate with the shelving and beveling from the inside out.

Entry wounds from *shot* at close range differ in no material way from entry wounds from bullets except in being of larger size The body sustaining the force of the muzzle blast is split open There is not likely to be an exit wound of any kind The tissues are torn and blown away, and if the part hit is covered with clothing, shreds of cloth are blown into the adjacent tissues As the range increases, the charge of shot spreads so that a shot spread of 18 to 20 inches will have been fired from a 12-gauge shotgun with modified choked bore at a range of 20 yards However, no exact opinion should be given until trial shot patterns are made by trial shots fired from a particular weapon and recorded The tattooing distance of a shotgun is the same as that of a rifle It is about 1 yard

The wounds inflicted by small arms are most frequently caused accidentally by "unloaded" arms The brief descriptions of these wounds as given here will be helpful in the recognition and treatment In cases of suicide and of murder the physician may be expected to give an opinion in answer to such questions as: Could a particular wound be inflicted by a certain weapon which is at hand? If so, at what range and direction was it fired?

A suicidal wound can only be inflicted from a range within the subject's reach (except when some string or cord is rigged up to pull the trigger). This range, for practical purposes, is 3 feet This range of 3 feet is also the range of the powder tattooing The length of shotgun and rifle barrels varies from 26 to 32 inches and therefore, for practical purposes, unless some sort of preparations for firing these arms is made, suicidal wounds will be made with muzzle against the part and from angles of fire not likely to be obtainable in a homicidal wound If a suicidal wound is inflicted at greater ranges, evidence such as a stick, string or some object used to pull the trigger will be found The significance of these objects in making the diagnosis of suicidal wounds is great and they and the method in which they may have been used should be looked for The significance of these objects may naturally escape the inexperienced police officer, and the doctor should ask about them himself

Self-inflicted wounds of a deliberate suicidal character are almost always contact wounds, situated in the sites of election, the right temple (or the left temple in left-handed persons), center brow, the roof of the mouth, and over the heart. An entry wound situated off an elective site always arouses suspicion of foul play. When, in addition, such a wound is inflicted from a range outside arm's reach, suspicion grows stronger Only the addition of some circumstantial evidence can decide the problem of the single wound not bearing the stamp of suicide It is rare for a suicide to be able to fire twice in any of the sites of election, for each is vital Two or more wounds almost certainly mean homicide.

Wounds inflicted by shotguns are greatly modified by sawing off a part of the

while using sharp instruments, in homicidal attacks and in suicide or suicidal attempts. Accidentally incised wounds from broken glass have no topographic preferences Wounds inflicted while using sharp instruments occur on the face, hands and feet. Homicidal wounds occur on the hands, face, neck, back and abdomen of the opponent, whereas suicidally incised wounds are topographically situated.

The person with suicidal intent often makes several superficial stroking cuts over wrists, neck, chest, abdomen, groins and legs in the belief that vital arteries lie superficially in these regions. Often these wounds do not even divide the skin After the disappointment of finding out that these vital structures are more deeply situated, a determined stroke is made which severs every tissue down to bone in a wrist, neck, chest, groin or leg Often in suicide by cutting the throat the carotid arteries may not be cut, for in the greatly extended neck the carotid arteries are displaced laterally to the spinal column and thus are spared because the knife impinges on the vertebrae before it can reach them.

Stab or *penetrating* wounds may be made with but little effort with sharp-pointed or sharp-edged weapons or with considerable effort with blunter-pointed instruments such as knives, forks and nails. The entry wound in either case is a slit Rocking of the weapon or twisting of the victim may tear such slits more widely. The deepest wound inflicted by a rotary movement provides an estimate of the minimal length of the blade.

It is the depth of the stab or penetrating wound which makes the injury dangerous Such a wound furnishes poor drainage and is susceptible to infection by the various clostridia (*Clostridium tetani*). A vital injury or a lethal infection by *Clostridium tetani* may have entered the body through a very small entry wound

Stab wounds are common to both suicides and homicides. Stab wounds inflicted by one with suicidal intentions are situated in the region of the heart or the epigastrium where the heart beat can be felt The suicidal stab is a single, deep penetrating wound made without rocking of the knife after entry. The homicidal wound is often finished with a rocking movement. The homicidal wound rarely is situated directly over the heart. It may be situated in the epigastrium or anywhere over the thorax. Multiple deep stab wounds in the back are homicidal.

The two types of *firearms* of small caliber commonly used for hunting of small game inflict accidental wounds as well as the wounds resulting from crimes of violence. These arms include those with rifled barrels (pistols and rifles) and the smooth-bored barrels, or shotguns.

A bullet wound from a rifled barreled gun consists of an entry wound and often an exit wound. The *entry wound* made by a *bullet* at close range bears the marks of everything that is discharged with explosive force from the muzzle. Its size varies with the caliber of the weapon

The entry wound which is made with the muzzle of the firearm from 6 inches to 2½ feet from its mark is split and scorched; the hairs are singed, maybe slightly blackened, and there are finely tattooed, unburned particles of powder embedded in the surrounding skin. The tissues beneath the skin are often torn away from their supporting structures. They may be tinted cherry red by the carbon monoxide in the gases which have been forced into them.

A discharge made more than a yard from the body will inflict the same sort of wound for ranges up to some 60 (pistol) to 200 (rifle) yards; the entry hole is split and soiled by the irregular vibratory course of the blunt end of the bullet in its trajectory. These entry wounds are soiled by the spin of the bullet. The oncoming bullet produces a *soiling ring* which distinguishes its entry from its exit When the momentum of the bullet is small, it may remain inside far removed from its *normal* trajectory.

Diagnosis is based on the history and the short duration of the illness, from 2 to 10 days The fever subsides within a period of a few hours up to two days

Bagassosis. The inhalation of bagasse dust, derived from the pulp of sugar cane after it has been crushed and the juice extracted, incites a pathologic process which has been called bagasse disease of the lungs or bagassosis Bagasse or sugar cane pulp is being used extensively in the manufacture of insulating building materials and refractory brick It constitutes a serious hazard unless properly handled

The etiologic basis for bagassosis is obscure Whether or not the pathologic reaction is due to fungi, bacteria or a virus associated with the pulp dust, to an allergic response to the bagasse or its possible infectious agents or their products, to some chemical or physical property of the dust or to any combination of these factors has not been determined.

Pulmonary changes incited by the inhalation of bagasse dust consist in a diffuse infiltration and consolidation, an acute bronchiolitis or a pneumonia which is similar to that seen in pneumoconiosis but which in one respect is greatly different It is a reversible reaction, with the process undergoing resolution and the lung regaining its normal appearance on the roentgenogram, a phenomenon which is not observed in pneumoconiosis

About 2 months of exposure to the dust are required before symptoms develop The onset is insidious and gradual The disease manifests itself as an acute febrile illness with extreme shortness of breath, a persistent cough with scanty mucoid sputum, and profound weakness.

Examination reveals a bronchopneumonia

The diagnosis is made on the basis of the history, findings on physical and roentgenologic examination, and the final clearing of the process in the absence of other causative factors

Thresher's Lung (Bronchomoniliasis) Thresher's lung is caused by the inhalation of dust from molded ("burned") grain Cultivation of samples of sputum on Sabouraud's medium yields *Monilia,* a yeastlike fungus In the severe instances of the disease the onset is sudden, accompanied by shivering, fever, malaise and cough with mucopurulent or sanguinolent expectoration, and dyspnea Ocular symptoms and rhinitis also may be present The clinical signs include a bronchial catarrh at the bases with dry subcrepitation, mild leukocytosis and an increased sedimentation rate The findings resemble those of miliary tuberculosis. In severe illnesses the densities increase and merge into a disseminated patchy fibrosis with bronchiectasis

Lipid Pneumonias Young children who resist the administration of oily vitamin preparations often inhale these substances into the lungs These oily preparations are often composed of fish oils irritating to the lungs However, these oils can be absorbed into the body from the lungs. Mineral oil is a saturated hydrocarbon It cannot be ingested into the body tissues and consequently it remains in the lungs indefinitely, except for the small amounts which appear in the sputum

Anatomic defects in the mouth, palate, tongue, larynx or esophagus, neurologic disturbances that interfere with swallowing, the use of forced feedings, and the fact that mineral oil, being bland, does not initiate the cough reflex, are factors that predispose to the aspiration of oil. Mineral oil pneumonia in adults often results from nose drops or nasal sprays When mineral oil reaches the dependent portions of the lungs, it first remains free in the alveoli Then some of it is phagocitized by the macrophages, some is disposed of in the sputum, and a small amount reaches the lymph nodes, but the bulk remains indefinitely in the lung, where it provokes the development of fibrous tissue The lower lobes, particularly the right, are most likely to be involved

The symptoms are those of a chronic pulmonary affection.

On examination there may be the physical evidence of consolidation The oil may be discovered in the sputum

The diagnosis of lipid pneumonia depends on the history and on roentgenologic

barrels or by removing the shot from the cartridge and reloading with slugs (irregular-sized pieces of lead or steel). These wounds are almost always homicidal wounds.

PHYSICAL AGENTS OF DISEASE

A physical agent, as defined here, is a material perceptible to the senses which produces disease by its presence It remains aloof from the chemical processes of the body and does not depend on the body for sustenance

Particulate Matter. Finely divided physical material may cause injury to the skin, to the mucous membranes and, particularly when inhaled, to the lungs.

Organic Particulate Matter. *Large quantities of organic dust, such as corn* meal, wheat flour, and coal dust, may be inhaled, sometimes causing clogging of the smaller air passages and resultant regions of atelectasis.

The inhalation of dust and smoke of cities may cause a mild form of pneumoconiosis In fact, evidence of it may be found on roentgenologic examination or at postmortem examination of the lungs of many adult dwellers in cities. The older such persons become, the more marked are these findings.

Smokes such as diphenylaminechlorarsine and diphenylchlorarsine may produce irritation of the nose and throat. The nasal accessory sinuses also are involved The symptoms consist of pain and a feeling of fullness in the nose and sinuses with severe headache. Later there is intense burning of the throat, with tightness and pain in the chest There are lacrimation, violent sneezing and marked nasal secretion. Nausea and vomiting also may occur Mental depression may be so severe as to cause the sufferer to inflict self-injury. All symptoms usually disappear in one or two hours, leaving no permanent injury Prevention consists of the use of the gas mask.

There are organic contaminants which cause coniotoxicosis, irritation of the respiratory tract, resulting in bronchitis, hay fever and asthma. Organic dusts are not indicated as being harmful unless a person becomes sensitized to them. For example, the pollens of various trees and plants, and vegetable dust, including that of wheat, corn, oats and barley, may cause asthma when inhaled by sensitized persons (see Chapter 18)

However, there are organic dusts which may cause irritation from the physical properties of the dust or from bacteria contained within the particulate matter, for example, the cotton bacterium in raw cotton

Byssinosis or Cotton Disease An acute illness, the cause of which has not been completely elucidated, occurs among rural mattress makers who use cotton in their manufacture. Probably the same disease is the so-called *mill fever* or *Monday fever* formerly found in workers in cotton mills The disease or diseases follow the inhalation of dusty cotton during the initial stages of cotton processing

The symptoms and physical manifestations described for this disease indicate that the severity of the illness is dependent on the presence and concentration of the cotton bacterium or its products in the cotton dust inhaled, and on the duration of exposure Neither age nor sex seems to influence the incidence of the disease.

These illnesses commence from 1 to 6 hours after work is begun. The initial symptoms are fatigue and generalized aches, followed by anorexia, headache, nausea and vomiting, the latter lasting 6 to 9 hours in some instances About 6 hours after exposure a sense of chilliness supervenes, followed usually by definite chills, fever and headache. In some patients the temperature may be 102 F (38.8 C) or more. Fatigue and generalized aches last from 2 to 4 days Many patients complain of abdominal pain or cramps and of substernal discomfort or pressure, varying in intensity and duration. The patient may be unable to take a deep breath

On examination the lungs are clear. There is a moderate leukocytosis. Results of roentgenologic examination of the chest are negative.

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The symptoms are those of a chronic pulmonary affection

On examination there may be the physical evidence of consolidation. The oil may be discovered in the sputum.

The diagnosis of lipid pneumonia depends on the history and on roentgenologic

examination of the chest when there are no other causes for the findings. The presence of fat in the sputum is not necessarily diagnostic, for fat may be demonstrated in almost any unfixed sputum stained with Sudan III and examined microscopically. The average concentration of fat is greater in bronchial sputum than in that obtained from the mouth. There is no correlation between the amount of fat and the type of pulmonary disease which may or may not be present. Recent ingestion of oil will cause no increase in concentration of fat, but increased amounts of fat are present shortly after intake of food.

Inorganic Particulate Matter. The term pneumoconiosis designates a chronic fibrous reaction in the lungs due to the inhalation of particulate matter (dust). It is attended by fibroid induration and pigmentation The condition in the lung may be designated according to the kind of dust inhaled, for instance anthracosis, asbestosis, siderosis, and silicosis Illnesses due to mixed dusts are designated by terms indicating the offending dusts, for instance anthracosilicosis and siderosilicosis.

Coniofibrosis is a form of pneumoconiosis characterized by a profuse growth of connective tissue due to a specific irritant It embraces silicosis, silicotuberculosis and asbestosis

Anthracosis and *siderosis* act principally by obstructing the lymphatic structures and impairing lymphatic drainage. An impaired drainage of lymph lowers the resistance of tissue and thus enhances any infection which may be present at the time or which begins thereafter.

Persons exposed to field, farm and road dust can, but rarely do, inhale enough dust to result in changes in the respiratory tract.

Silicosis Silicon dioxide is abundantly present everywhere. The natural defense mechanism of the lungs protects them against even high concentrations of silica dust. Those whose nasal passages have been injured by trauma, surgical operation or disease are more readily susceptible to silicosis than others.

The ciliated epithelium of the trachea and bronchi directs much of the dust lodged in these tubes to the pharynx where it is swallowed or expectorated Particles larger than 10 microns in diameter cannot enter the terminal bronchioles It is therefore the particles of silicon of less than 10 microns in diameter which can pass into the smallest bronchioles and lodge in them

Silicosis produces a wide range of lesions, all of which serve to retard the flow of lymph with an attending extensive fibrosis in both lungs.

In most instances of rapidly developing silicosis the lesions of pulmonary tuberculosis are present. Grossly the appearance of the lungs is not that of silicosis but suggests the induration of organized pneumonia The tracheobronchial lymph nodes are not enlarged No nodules are visible on the cut surface of the lung or on the pleura. There is diffuse thickening of the alveolar septa

There is present a high incidence of cardiac failure in silicosis

There is no evidence to indicate that pulmonary malignant disease develops more frequently among silicotic patients than among other persons.

Silicosis is not necessarily a progressive disease. Workers in dusty trades often have been frightened by what they have heard and read about silicosis and few consequently are those who do not have symptoms. Symptoms will surely follow if these persons are made aware that the roentgenograms reveal changes in the lungs.

The symptoms of silicosis depend on the stage of development of the disease. A history of 2 or more years of exposure to dust (10,000,000 or more particles of dust less than 10 microns in diameter, of which 25 to 35 per cent is free silica, per cubic foot of air) is required for the acquirement of silicosis In most persons silicosis never gives symptoms

As silicosis progresses sufficiently to cause symptoms, there are *shortness of breath* on exertion and a slight nonproductive cough. As silicosis *advances further*, the shortness of breath becomes severer. When the pleura is involved, pleural pain

occurs. A dry cough is frequently present. If any sputum is present, it is in small amounts.

Rapidly developing silicosis or *acute silicosis* occurs in those who are exposed to large numbers of finely divided particles of almost pure silica dust, as may occur in sandblasting or pulverizing plants. The symptoms of a rapidly developing silicosis are those of bronchopneumonia As the pneumonia lingers on, it is then found that there is present in addition to the acute silicosis some other pulmonary infection, usually tuberculosis

Silicosis may be suspected from the physical signs plus roentgenologic findings indicating silicosis.

On examination there may be limitation of movement of the thoracic wall during forced respirations This limitation of motion is confirmed by palpation The percussion note may be dull over localized regions of the thorax. Scattered rhonchi are sometimes heard on auscultation, and expiration is prolonged. On examination by physical means the findings in those who have a rapidly developing silicosis are those of bronchopneumonia.

The diagnostic requirement of silicosis is the presence of shadows on the roentgenogram which might be due to silicosis Diagnosis of disabling silicosis without disabling symptoms is impossible

The diagnosis of clinical or disabling silicosis is based on the degree of dyspnea, thoracic pain and cough The roentgenologic findings may or may not be far advanced in those who have clinical manifestations of silicosis.

Silicosis and Pneumonia A patient who has symptomless silicosis may have pneumonia, but perhaps is no more likely to have it than anyone else of the same age group The severity of the pneumonia may not be enhanced by the presence of silicosis though there is no agreement on this point

Silicosis and Tuberculosis. Pulmonary tuberculosis in the presence of silicosis is known as silicotuberculosis The patient who has silicotuberculosis can live and get along, with proper care, the same as anyone else who has tuberculosis

Tuberculosis is more prevalent among industrial workers, even in the absence of hazardous dusts, than among the general population. Until recently, however, almost no attempt was made to protect individuals in industry against their tuberculous fellow workers For this reason alone the incidence of tuberculosis should be higher among persons in dusty occupations than among the general population.

Siderosis Excessive iron in the lungs is termed siderosis. Iron may accumulate in the lungs to such an extent that approximately 8 per cent of the weight of the moist lung will be iron The source of iron in the lungs is often electric arc welding.

The steel electrode consists of approximately 99 per cent ferrous material with extremely small amounts of such alloy substances as carbon, manganese, nickel, phosphorus and silicon The coatings are composed of such materials as aluminum, borates, chromium, fluorides and silicates The fumes arising from coated rods consist largely of extremely small particles of iron oxide

As in silicosis, symptoms rarely occur. If symptoms are present, they are dyspnea, thoracic pain, and perhaps a cough

There is a great similarity of the roentgenologic appearance due to the deposit of iron oxide and that due to silicotic nodulation

Silicatosis The dust responsible is talc in the form of tremolite (calcium magnesium silicate) or soapstone (hydrous magnesium silicate), or both, since free silica or other dust in a high concentration is not found Tremolite talc is chemically much the same as asbestos The principal difference is in the physical rather than the chemical structure

The symptoms of the workmen consist of dyspnea, cough, thoracic pain, and weakness After disability occurs, recovery apparently is impossible. On roentgenologic examination there is diffuse haziness, but general nodulations are absent.

Asbestosis. Asbestosis is characterized by diffuse interstitial pulmonary fibrosis and the presence of asbestos bodies in the lungs.

When particles and fibers of asbestos are inhaled a pulmonary fibrosis results from their entrance As the condition progresses, extensive fibrosis develops. Walls of the alveoli become thick enough to reduce the alveolar capacity. The visceral pleura is thickened

At first there are no symptoms, but as the condition progresses, shortness of breath may occur which late in the disease may be distressing. Cough at first is mild, but later it becomes severe and is productive of tenacious sputum which at times is blood streaked There is substernal thoracic pain.

Examination by physical means reveals no important findings until the advanced stages of the disease are reached In the advanced stages a dull percussion note may be elicited over the lower two thirds of the lung fields Auscultation reveals diminished or feeble breath sounds and expiration is prolonged. Dry, crackling, or even moist, rales may be heard over the lower half or two thirds of the lungs.

The diagnosis of asbestosis requires a history of long-continued inhalation of asbestos dust in addition to the roentgenologic findings in the lungs.

Irradiation Injuries. The term radiation hazard is indicative of the dangers associated with ionizing radiations and the radiant energy from heat and light. The injury from radium is comparable to that arising from the roentgen rays The undesirable effects of ionizing radiation rarely become apparent after the use of the roentgen rays in diagnosis Undesirable effects are more likely to become apparent from the use of roentgen rays and radium in therapy

All types of ionizing radiations produce destruction of cells. From a biologic viewpoint, roentgen rays, gamma rays, alpha and beta particles and neutrons differ essentially only in the distribution and the magnitude of the destruction produced

Radiation Reactions. Incidence of sickness due to roentgen rays varies with the patient and also with the kind of disease for which treatment is being administered Patients receiving treatment for the lymphoblastomas occasionally complain of a disagreeable taste in the mouth almost immediately with the start of treatment Nausea and vomiting may follow the administration of but 100 r. Other patients with other tumors frequently withstand 400 r doses without being upset. Profound fatigue also occurs as a sequel to radiation treatment The roentgenologist is aware of the danger and does all that is possible to prevent severe reactions.

Edema following irradiation may be manifested early or late Early edema may be manifest from an hour to several hours after irradiation Late edema due to obstruction of lymph drainage is a serious sequel to irradiation Edema indicates that the irradiation reaction has advanced beyond the desirable limits

Erythema after irradiation has a latent period of 2 to 10 days Varying amounts of roentgen rays, depending on the method of application, when administered in a single dose will produce erythema, as well as epilation, in many skins

A *factitial dermatitis* may follow the erythema Such a dermatitis is characterized by progressive ulcerations of the skin The affected skin is a hard, thickened scar Over the scarred skin course numerous dilated veins

Severe radiation ulcers are the late results of overdosage or are due to an increased sensitivity of the patient or both. These ulcerations are due to the ischemia resulting from destruction of vascular endothelium. They are painful, indolent, and may be permanent Indurated ischemic tissue may become nonviable and ulcerate 2 or 3 years after the last treatment Epithelioma may arise as the last complication of irradiation injury

A distinction is made by the roentgenologist between severe radiation reactions of skin or mucous membrane which are intentionally caused in carrying fractionated radiation dosage to a high level, and painful, deep, nonhealing ulcers that are the result of gross unintentional overdosage or of ill-advised repetition of massive doses

In the administration of a protracted course of roentgen therapy the roentgenologist plans to obtain epidermal effect, epithelitis, epidermitis, and mucositis, without irreparable injury to cutis and subcutis This means a prominent hyperemia, frequently with blisters, denudation, and formation of false membrane. However, recovery from these reactions will ensue without undue induration, and the epithelium will regenerate rapidly.

Irradiation Injury to the Intestine From Treatment for Carcinoma of the Cervix. The intestinal mucosa is so susceptible to injury from irradiation that it sometimes is difficult to deliver a sufficient amount of radiation to destroy the malignant process in the uterus and still prevent excessive, harmful, secondary effects of irradiation from developing in the rectosigmoid and ileum.

Conditions predisposing to excessive exposure of the intestines to irradiation include retroverted uterus, uterus with a thin muscle wall, and peritoneal adhesions fixing one or more loops of intestines in the pelvis where they are likely to receive a concentrated dose of irradiation Irradiation therapy is given cautiously to those who have had pelvic infections or previous surgical operations in the pelvis

The mucosa of the intestines usually manifests irradiation injury by an acute inflammatory reaction consisting of edema, hyperemia, and spasm This change may occur at any time during the course of therapy, or 1 to 2 weeks after completion of the treatment There may be direct injury of the blood vessels manifested by endarteritis, thrombosis, and subsequent infarction of the involved portion of bowel The mucosa may then ulcerate The ulcerations consist of single or multiple, irregular, superficial erosions which progress to deep, discrete ulcers The surrounding mucosa becomes thickened and indurated, and telangiectasis ensue

As the lesions heal, bands of scar tissue form which may constrict the bowel and produce obstruction In some the primary irradiation injury may involve the perirectal tissues, with subsequent production of a diffuse mass of fibrous tissue involving all pelvic structures and producing a condition difficult to differentiate from a pelvis filled with carcinoma

The symptoms of irradiation injury to the rectosigmoid or the ileum may appear within the first month after the institution of therapy, or years afterward.

In many, however, there is only mild rectal discomfort with very little or no bleeding When the symptoms are severe they consist of: (1) those arising from proctosigmoiditis and (2) those referable to obstruction of the lower part of the small intestine

The symptoms referable to the proctosigmoiditis are first of all blood in the bowel motion, which is attended by pain, tenesmus and frequent rectal discharges of bloody mucus. In instances of severe injury the rectal hemorrhage is uncontrollable by ordinary means and requires many blood transfusions in order to sustain life

In a great many pain in the pelvis and rectum is severe, and often drug addiction is acquired

Ileal involvement is rarely present without rectosigmoidal changes When ileal symptoms are present, they are manifestations of obstruction of the distal small intestine

On digital examination of the rectum the lumen of the bowel may be contracted and the walls of the rectum scarred When an ulcer or ulcers are present, they are oval or circular with discrete indurated margins On digital examination one of these ulcers is hard and indurated like a malignant ulcer. These irradiation ulcers sometimes perforate and lead to peritonitis, or to external fistulization or to fistulas into the vagina or the bladder

On sigmoidoscopic examination in the first weeks after treatment the mucosa is red and edematous Later, the mucous membrane becomes atrophic Telangiectases and contraction of scar tissue ensues

The diagnosis of irradiation injury to the intestines from treatment of carcinoma of the cervix is usually established by endoscopic examination In occasional in-

stances, however, it may be difficult to determine whether or not there is recurrence or extension of the cervical carcinoma. If there is considerable perirectal fibrous tissue, it may be impossible to know whether there is recurrence or metastasis of the carcinoma

The Nervous System. Therapeutic irradiation over the pelvis during pregnancy is dangerous to the fetus. Often microcephaly and idiocy are present at birth, seemingly from the effects of irradiation of the fetus.

Extensive and prolonged irradiation of the head after birth may also cause destructive changes in the brain There is an early inflammatory reaction which begins to recede in 4 or 5 weeks A late reaction may begin as long as 1 to 7 years after the irradiation This reaction may appear in widespread regions of the brain It consists of necrosis apparently due to injury to the blood vessels.

Malignant tumors of the nose, mouth, pharynx, cervical lymph nodes, esophagus, middle ear, parotid gland, and lesions of vertebrae often require irradiation treatment. In instances of increased susceptibility or overtreatment injury from irradiation may be as dangerous as the lesions themselves. Because of the long latent period between the irradiation and the appearance of symptoms, the cause of the condition may not be immediately apparent.

The manifestations of irradiation injury seem to be due primarily to injury to the blood vessels rather than to the neurons, and the eventual neurologic lesions seem to be the result of gradual impairment of blood supply.

Symptoms may be ascribed, without proof, to metastatic lesions from the original tumor or to cerebrovascular accidents The symptoms commence with numbness and tingling in the hands or feet precipitated by flexion or extension of the neck and often associated with pain in the neck and shoulders In mild injuries these symptoms are transient and disappear in 3 to 9 months In the more seriously affected spinal cords the paresthesias are followed by weakness or spastic paralysis and later by dysfunction of bowel or bladder. Death results often from bronchopneumonia or ascending infection of the urinary tract Cranial nerve palsies, ataxia, and hemiplegias in older patients cannot be differentiated from those due to cerebrovascular accidents.

The lesions of irradiation myelitis often can be distinguished from those of metastasis to the spinal column or to the cord by the absence of roentgenographic changes in the vertebrae and the absence of changes in the spinal fluid

Acute Radiation Syndrome. The acute radiation syndrome is caused by sudden exposure to the actions of the roentgen rays or of the penetrating radiations liberated by radium or the atomic bomb The resulting changes depend on the inherent sensitivity of the exposed tissues and the type of radiation and are attributable to injury to formed elements of the blood and the blood-forming organs, the endothelium of blood-vessels, and the digestive tract and the uterine cervix These particular tissues all show a tendency toward ultimate regeneration, and it is on this fact that present therapeutic programs for the supportive treatment for malignant disease of these tissues are based.

The effect of irradiation on the body is a cessation of mitotic activity and death of cells which are not immediately replaced The time required for this destruction depends on the susceptibility and the life span of the cell in question. Cessation of mitotic activity by the leukopoietic tissues results in leukopenia within 24 hours The lymphoid cells also rapidly disappear, but less rapidly than the granulocytes. Destruction of the erythrocytes is the last of the hematologic alterations to appear. Subsequently the marrow may assume a hyperplastic appearance with arrest of maturation

Changes in the oral and pharyngeal membranes and the gastrointestinal tract are restricted to the mucosal surface and consist of ulceration and sloughing These changes result from a combination of the effects of radiation and the rapid invasion of microorganisms

The gonadal epithelial tissues of boys and men are extensively destroyed. The female gonads are less easily affected.

Three forms of radiation sickness are categorized. 1 *Initial shock* occurs in those who have received overwhelming injury, as from an atomic bomb. Vomiting appears within 12 hours after exposure and within 24 hours, owing to the effects of vomiting and radiation, prostration, fever and diarrhea follow.

On examination weakness, tachycardia and hypotension may be present in the extremes. Petechiae and purpura are present after about 5 days. Toward the end of the first week after the injury the fever increases rapidly and the temperature may reach 104 F (40 C) The pulse rate is fast and the pulse is enfeebled. The weakness is extreme. *The profuse and often bloody diarrhea contributes to the dehydration* Examination of the blood reveals progressive leukopenia that may reach levels of 400 to 500 cells per cubic millimeter. The erythrocytes usually remain normal, but the platelets are depressed in numbers

Death occurs in from 1 week to 10 days

2. The *acute form* occurs in those who have incurred extensive but often not fatal injury Within 24 hours after exposure, nausea, vomiting and diarrhea with prostration usually appear and persist for a day or two The patient is then generally well for 10 days to 2 weeks, at the end of which time great weakness, malaise, petechiae, purpura of skin and mucous membranes, and epilation of the scalp and perhaps of other areas of the body occur These lesions of the mouth and pharynx resemble the lesions of agranulocytic angina Gastrointestinal disturbances, of which diarrhea is the most pronounced, reappear and there is fever Death often occurs in 3 or 4 weeks. Those who survive the exposure enter a more chronic course with continuing ulcerative lesions and anemia Recovery slowly progresses, or the patient succumbs to infection

3. The *subacute form* of radiation sickness occurs in persons who have been less severely exposed than those who have the acute form This subacute form of the disease consists of the severe reactions which occur in those who have had large exposure to roentgen rays for treatment and are more susceptible to the effects of irradiation than is expected Often such sickness cannot be avoided Three to 5 weeks after initial exposure, epilation occurs, to be followed by mild inflammation of the oral and pharyngeal membranes and weakness with malaise A watery diarrhea develops The hematologic changes in these patients are often those of severe and increasing anemia If death occurs, it is due to aplastic anemia, occurring 2 to 4 months after the initial exposure A large number of patients in this group recover

Injuries and Death from Electric Currents and Lightning. ***Electrocution.*** A voltage of 60 may cause death if the amperage is high, but it is seldom that a fatal result ensues from a current of less than 230-260 volts

Shock from the sudden passage of a current of low voltage (60 V) and high amperage, when the head or the chest is imposed between the contact and the ground, as may be present in the home, may cause death Instances of death from low voltages are likely to occur in the bathroom or in the basement of the home. Death there is produced by prolonged contact and ventricular fibrillation

In instances of shock and death from contact with a high-voltage current, the fatality is likely to be caused by the discharge of current through the body and ventricular fibrillation rather than by burns If resistance through the body is low, burns will not ensue.

When a cutaneous burn is present, it may be so small as to be difficult to locate in the area of cold white skin which surrounds the point of contact of the current with the skin Cutaneous wounds of fantastic configuration may be sustained when there is a sudden or an intermittent contact with high-voltage electric currents

The postmortem findings away from the points of contact may be entirely absent

In those who have died from cardiac ventricular fibrillation there are dilatation of the chambers of the heart, sometimes with petechiae under the pericardium and ventricular endocardium, and gross pulmonary and afferent venous congestion and cyanosis.

Lightning. Lightning stroke or death from lightning is economically important from the standpoint both of loss of human life and of the loss of livestock Nine hundred to 1,000 persons die in the United States each year from lightning The number of livestock lost by this means is much greater.

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Instant death is the result of either paralysis of respiration or fibrillation of the ventricles of the heart In instances of serious shock, even though artificial respiration is maintained for hours, death may ensue

In those who survive, there may be unconsciousness for a variable period In some cases consciousness is never regained and death occurs during convulsions days later. If the patient survives, there may be various mental disturbances, blindness, and palsies, probably from a prolonged cerebral anoxia which follows the shock.

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Effects of Excessive Sunlight. The effects of sunlight, due to the differences in the amount of pigment in the skin, vary greatly in different persons The albino has no pigment in the skin and thus is very susceptible to short exposures to the sun of summertime

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of the skin, but if the threshold value is greatly reduced, the sensitivity is usually regarded as pathologic. A photosensitizing substance may be present in the individual or it may enter artificially in the form of medicine or food or may come from contact The photosensitivity dermatoses may be divided into photo-allergic cutaneous reactions and photodynamic manifestations.

The *photo-allergic reactions* are observed rarely away from temperate climates, where in some persons the allergy recurs every year with the onset of the sunny season. The terms urticaria solaris, eczema solare and prurigo aestivalis indicate their seasonal incidence. Photo-allergic reactions are not conditioned by previous exposure to light; that is, allergy to light is defined as one in which the allergic manifestations occur on the uncovered skin

The photodynamic manifestations depend on a photosensitizing substance naturally present, such as porphyrin On exposure of the sensitive person to sunlight, hydroa vacciniforme, hematoporphyrinuria or xeroderma pigmentosum ensues.

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In a susceptible person *solar urticaria* may result from a brief exposure of the skin to sunlight Exposure is followed in a few minutes by development of intense itching and erythema limited precisely to the areas exposed to the sunlight Soon small urticarial lesions form in the erythematous area and these quickly coalesce to form a continuous urticarial wheal confined to the exposed area When the urticarial edema has developed, a flare of diffuse erythema surrounds the wheal of the exposed skin

Hematoporphyrinuria is discussed in association with the disease porphyria (Chapter 22)

Xeroderma Pigmentosum. This rare, and fatal, disease occurs in red-haired persons The disease is due to an altered reaction of the skin to light. The disease may commence in childhood or after adulthood is attained. The manifestations are the same in either children or adults

In children the dark brown freckles persist after summer is over. The skin begins to atrophy, telangiectasis appears and the skin begins to look old As the senile appearance of the skin develops the muscles become atrophic and weak, completing the appearance of old age In a few years warty growths arise, some of which turn malignant By the time adolescence is attained the patient dies from a disseminated highly malignant epithelioma

A more rapidly progressive form of the disease, beginning in adult life, may occasionally be encountered after undue exposure to sunlight. Often the disease occurs after undue exposure of the skin to sunlight by visitors to winter resorts Muscular atrophy is absent in the adult form of the disease.

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Sun and wind combined produce a prolonged irritation to the skin which thickens, dries and wrinkles it This type of weather-beaten skin is observed in farmers, ranchers and sailors. If such a skin becomes hypersensitive to light, symptoms occur at first only in the height of summer. As the degree of sensitization increases, the disease appears earlier year by year, until even in winter some trace remains

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and the arrhythmias which are produced tend to remain during recovery until the myocardium is again well oxygenated. However, the brain is affected by anoxemia before the heart is, and peripheral circulatory collapse can result from a deficient supply of oxygen to the central nervous system.

The effects from the progressive reduction in atmospheric pressure at higher altitudes result from the effects of the expansion of gases, from the pressure on the ear, or if great changes in pressure occur, from the changes in the volume of gases contained within the body. The coefficient of the expansion of gas under reduced pressure is such that a volume at 18,000 feet is double the size it was at sea level, four times that of sea level at 34,000 feet, and six times as much at 42,000 feet

Aero-otitis Aero-otitis is due to rapid changes in pressure difference between the cavities of the ears and the surrounding atmosphere.

Aero-otitis Externa Aero-otitis externa occurs when a person has used tight ear plugs in descent from high altitude flying or when one has severe rhinitis associated with postnasal infection. It is characterized by hyperemia and ecchymotic hemorrhages affecting the tympanic membranes and perhaps the soft tissues of the external auditory canal

Those who have flown despite the presence of a rhinitis should be treated if the pain in the ear or ears persists for more than an hour or two after landing

Aero-otitis Media. Aero-otitis media occurs when there has been rapid change in pressure differences between the middle ear cavity and the surrounding atmosphere. Usually the eustachian tubes are not patent or are partially obstructed. It is a traumatic inflammation of the middle ear

The well-known devices of keeping the pressure difference equalized by keeping the eustachian tubes open are gum-chewing, swallowing, yawning, eating and drinking. In children the same end is attained by having them inflate small balloons, and feeding infants during descent

Aerosinusitis may develop in those who have sinus disease.

Airsickness. One of every 10 adults may be affected by airsickness It is the same as motion sickness

As preventive measures against airsickness, pregnant and neurotic women and persons with gastrointestinal disease and those who are convalescent after abdominal operations are advised to have adequate sleep on the preceding night, bowel evacuation, a light meal one hour before flight, small light meals during flight, warm clothing, ear plugs to minimize noise, to assume a recumbent position, and to look up to minimize stimulation of utricles by otoliths

Abdominal Distention Persons contemplating flights at high altitudes are advised to abstain from ingestion of foods which they think form gas and not to partake of carbonated beverages The precautions already mentioned, of adequate rest, easily digested foods, and good bowel evacuation, are also good prophylactic measures against abdominal distention Patients who have intestinal obstruction generally should not be transported by air

Mountain Sickness. On ascending the mountain side to heights of from 12,000 to 15,000 feet, owing to a low atmospheric pressure of oxygen which occasions oxygen want in the tissues, cyanosis, nausea, headache, intestinal disturbances and hyperpnea develop If exercise is continued, syncope may ensue

After acclimation at these altitudes, symptoms are not present unless physical exercise is performed During and after even mild physical exercise there are dyspnea, blue lips and ears, and often periodic breathing When acclimation is present, the alveolar carbon dioxide pressure is reduced to 25 to 30 mm., which increases by about 50 per cent in the ventilation of the lungs. This process of acclimation is associated with a great increase in the number of erythrocytes and in the hemoglobin Hemoglobin of 120 to 150 per cent may be attained (see Polycythemia, Chapter 12)

body from low altitudes to higher ones, as in airplane flight and (2) removal of the body from a high barometric pressure, as is present in a caisson, to a lower one, the surface atmosphere

The cause of the disability in the decompression sickness of divers, caisson workers and fliers is the same, namely, bubbles, consisting chiefly of nitrogen, which occlude veins, capillaries and, more rarely, arterioles, collect in tissues, especially fatty tissue, and cause pain by distorting nerves or nerve endings.

Decompression disease most commonly affects older persons and those who are fat. There is a *varying susceptibility to decompression disease among the young and* fit, and apparently this susceptibility varies in each individual from time to time. An occasional person seems to become more susceptible on subsequent decompression Likewise an occasional person seems to become somewhat adapted to decompression. There is some evidence to indicate that the incapacity is less likely to occur when the incentive is high One hour of preoxygenation prior to ascent decreases the incidence of incapacity.

In caisson workers exercise is the most important factor predisposing to bends and chokes

Owing to the rapidity of decompression in fliers on rapid ascent the symptoms come on more quickly than in caisson workers In the latter workers, since decompression is carried out more slowly, the symptoms often do not occur until some time after decompression (one-half hour to an hour and a half).

Often the symptoms are mild, with headache and uncertainty of gait which soon pass away In severe injuries the symptoms commence with pains in bones, joints (bends) and abdomen On inspiration there is a cough (chokes) Paralysis of the legs may ensue with disturbances of sensation Monoplegia or hemiplegia resembling apoplexy is rare In most patients these symptoms pass away, but in a few the coma deepens and death occurs Some of those severely injured who survive may be disabled by a persistent hemiplegia, monoplegia or other disability from injury to the spinal cord

On examination there may be coughing almost with each breath. *The coughs or* the chokes are apparently due to the collection of bubbles in the small branches of the pulmonary artery, and at times some enlargement of the right side of the heart may be detected Distention of the abdomen is not common The abdominal gas pains and distention are due to the expansion of gas in the stomach and colon and do not occur if the subject can readily expel the gas *There may be some fullness about* the joints which stiffens (bends) them and causes pains, especially if attempts are made to use the joints Bends are usually associated with collections of gas or bubbles in the veins or in the tissue of the fascial planes about the joints, tension being a factor in their production.

In more severe injury there may be neurologic findings the same as in monoplegia or hemiplegia Coma may be present

The diagnosis is usually obvious, and it is confirmed by the response to recompression The symptoms may occasionally recur or occur after recompression The prevention of the symptoms is the same in divers and in fliers, namely, *denitrogenation* or the removal of most of the liter of dissolved gaseous nitrogen, contained within the blood of normal persons, by the inhalation of pure oxygen for several [illegible] prior to exposure

[illegible]titudes. The stresses encountered during flight [illegible] 10,000 feet are not important Above 10,000 feet, supplementary oxygen is required in *increasing amounts.* At 40,000 feet, 100 per cent oxygen is inadequate unless it is supplied under pressure.

In persons whose ability to oxygenate tissues is hampered by respiratory or cardiovascular disease, the *effects of hypoxia* may become more apparent at higher altitudes than in normal persons, and the consequences may be serious. Anoxia dilates the heart,

The appearance of the body dead from asphyxia indicates to a certain degree the type and the duration of the asphyxia suffered. When asphyxia has developed gradually, there is a livid color of lips, face and ears When excessive carbon dioxide has accumulated, there is present a dark bluish tint. When death has followed anoxemia, the face may be pale. The tongue may lie in normal position, or the tip may be pressed against the back of the teeth. When asphyxia has been severe, as in acute pulmonary edema or in hanging, the tongue is protruded either between the margins of the teeth, or beyond them. A frothy and frequently blood-stained fluid may be present at the corners of the mouth and at the nostrils The conjunctivae are congested and speckled with small punctate hemorrhages.

The larynx and the trachea contain a varying amount of frothy watery secretion. The lungs are engorged and edematous. Petechial hemorrhages are commonly present in the parietal, pulmonary and pericardial pleurae, pericardium, heart muscle and endocardium. On section, a copious, frothy, dark-colored, blood-stained exudate is observed

The cavities of the right side of the heart and the venae cavae are engorged. The cavities on the left side of the heart are often comparatively empty.

The cranial sinuses are usually filled with dark-colored blood The brain is often congested and speckled with hemorrhages. An excess of serous fluid is present in the lateral ventricles

Asphyxia and Drowning The physician may be called upon to give an opinion in regard to death from drowning Usually the circumstances make the cause of death obvious, but not always A person may be said to have died from drowning into whose air passages and lungs air has been prevented from entering by the presence of any watery or viscid fluid which has been aspirated into the air passages and has caused asphyxia

The duration of the process of drowning varies from about 2 to 5 minutes. Occasionally a person on entering the water may die suddenly before the process of drowning has been properly initiated These deaths may be due to the sudden entry of water into the larynx or to the impinging of cold water on the nasal or postnasal mucous membrane, with ensuing powerful stimulation of the glossopharyngeal and vagus nerves, cardiac inhibition and death

When a person falls into water during a fatal syncopal attack in which respiration had ceased before submersion, the water will not be inspired, and the signs of asphyxia will be absent When a person falls into water as the result of an apoplectic or epileptic fit or a serious traumatic injury to the body, the immediate death will be due to drowning, the respiratory function having continued. The lesion which precipitated the fall and whether or not death was due to injury or to drowning can be discovered only by postmortem examination

The external signs found on a body recovered from water immediately after drowning consist of the presence of a fine foam or froth at the mouth or the nostrils or both Objects from beside the water or that were floating in it, or material from the bottom of the water, may often be found clutched in the victim's hands.

When a person who is unable to swim, or one who can swim but who is laden with heavy clothing or is fatigued, falls into water he sinks and inspires a mixture of air and water. Usually he rises to the surface again and expels the water and air This increases the specific gravity of his body, and he again submerges. Under water, he inspires more air and water. This initiates coughing, air and water are expelled, more water is inspired, and the lungs become progressively heavier, with the result that the tendency to sink becomes greater as this often repeated process of expiration and inspiration continues Finally the lungs become filled with water and the body sinks to the bottom, head downward

The blood passes to the head and neck. Since decomposition is enhanced by the presence of blood, it proceeds in the head and neck more rapidly than elsewhere,

Diseases Which May Contraindicate Flight by Air. Patients who have intestinal obstruction or impending obstruction, those who have cardiac or pulmonary conditions in which a reduction of oxygen or pressure may be detrimental, those in shock, and those who have severe anemia, maxillofacial injury, or cerebral injury should not be transported by air unless special attention can be provided and unless air pressure within the cabin is adjusted in relation to the altitude at which the plane is to fly.

Patients with angina pectoris should have an electrocardiogram to exclude an infarct, since infarction is a contraindication to flight by air for at least 60 days, preferably 6 months

Hypertension is not a contraindication to flight if the diastolic pressure is less than 110 mm. of mercury.

If a pulmonary disease has seriously reduced pulmonary reserve, flight is hazardous Many patients with disorders of the lungs, however, tolerate moderate altitudes if given oxygen during the flight.

Mild asthma is not a contraindication to flying. Tuberculosis usually is a contraindication. Rapid contraction and expansion of collapsed lungs are deleterious to healing, and tearing of adhesions attached to diseased lungs may cause hemorrhage or permit dissemination of the infection to new sites or to distant parts. If flight is necessary, sputum must be negative and cavities adequately controlled by collapse. Pneumothorax is an absolute contraindication, particularly if the volume of air is large and the area recently has been filled.

Patients who have undergone lobectomy or pneumonectomy do not travel well, especially within the first 3 months postoperatively Patients with pulmonary foreign bodies may fly but must be grounded at once if pulmonary edema is threatened.

Patients who have anemia are permitted to fly if hemoglobin is at least 60 per cent, leukemic patients should have at least 80 per cent hemoglobin

A diabetic person not readily subject to insulin shock or coma may fly. The attendant should be informed at the beginning of flight if a passenger has severe diabetes and has taken large doses of insulin

Agitated patients who might be dangerous, or obnoxious, or irritating should be absolutely forbidden to fly

Epileptic patients have a tendency to seizures aloft, and must be individually evaluated for the conditions anticipated during a specific flight.

Women may be flown without question during the first 8 months of pregnancy, provided there is no history of premature birth or habitual abortion

During the first 10 days of life the respiratory system is not sufficiently established to permit exposure to respiratory stress

Asphyxia. Asphyxia is essentially a state, or series of states, induced by deprivation of oxygen An asphyxia may proceed slowly and be characterized by gasping for breath and marked cyanosis with retention of carbon dioxide and depletion of oxygen In contrast to this type of asphyxia is that due to depletion of oxygen, or anoxia, characterized by skin pallor due to little or no retention of carbon dioxide.

Asphyxia originates from many causes, such as occlusion of the air passages, impediment to respiratory function by pressure on the thoracic wall, strangulation, suffocation, hanging, throttling, drowning, electrocution, and the inhalation of toxic gases; paralysis of the respiratory nerves or muscles; and from causes operating from the lungs or from the pulmonary circulatory system

When the asphyxial process is slight and prolonged, the congestive component will be diminished, when acute, lividity and congestion are extreme, and when, during the process of asphyxia, heart failure precedes respiratory arrest, the asphyxial signs may be less pronounced, depending at which stage in the asphyxial process cardiac arrest occurred.

This is more often used in resuscitation of children than of adults. Mouth-to-mouth insufflation is an ancient method of artificial respiration since it was possibly employed by Elisha in resuscitating the son of the Shunammite (II Kings, Chapter IV, Verse 34).

In recent years investigative work has been done to determine the relative efficacy of the various methods employed in artificial respiration In 1951 Gordon, Sadov, Raymon and Ivy recommended for general use the Nielsen method. These investigators seem to believe, however, that the Schafer-Emerson-Ivy (hip lift-prone pressure) method was the most effective of all methods. Since 1951 various organizations, such as the American National Red Cross, have approved or adopted the Nielsen method.

The preferable method of artificial respiration is determined by the circumstances under which it is to be employed and the experience and the physical condition of the operator. For instance, on removal of a body from the water of a swollen stream to a brushy, muddy, slippery bank, by one who is alone and exhausted it is well for him to know the importance of placing the asphyxiated person in a position so that his head is somewhat lower than his thorax, face down, the forehead placed in the palm of the victim's hand as in the Nielsen method. Despite exhaustion, the operator can usually muster enough strength intermittently to elevate the elbows and to push downward 10 to 20 times per minute on the lower back and ribs

The most important accomplishment to be obtained in resuscitation after immersion is removal of water from the lungs as rapidly as possible As the water is removed from the lungs the space occupied by it is filled with air. Therefore, artificial respiration is immediately urgent.

The *Nielsen method* (Fig 19-1) of artificial respiration requires that the victim be placed in the prone position with the forehead resting in the palm of one hand which is resting on the other. Percussions with the fist are administered between the scapulae to force the tongue back into position. The elbows are grasped and raised to cause active inspiration, they are then released, and pressure is exerted over both scapulae to produce active expiration The maneuver is performed rhythmically 10 to 20 times per minute. Undue pressure may fracture the ribs



After Gordon Fainer and Ivy, J A M A, 144 1455, 1950

Fig 19-1 The Nielsen method of artificial respiration.

The *Schafer (prone pressure) method* (Fig 19-2) is the simplest and for this reason it has been widely used as a method of artificial respiration. The patient is placed in the prone position with arms extended and face to one side Pressure is exerted with the hands close together on the lower portion of the thorax The pressure is rhythmically applied and relaxed at about the rate per minute of normal quiet respiration. The pressure on the thorax causes active expiration and passive inspiration as the result of elastic recoil of the lungs when the pressure is relaxed. The maneuver requires little muscular exertion by the operator.

The *Schafer-Nielsen-Drinker method* (Fig 19-3) requires that the patient be placed in the Nielsen position One operator performs the prone pressure procedure of the Schafer method while another operator alternately raises the elbows or arms. The Drinker method thus eliminates the pressure exerted over the scapular area in the

but the color changes which usually are observed in the lower quadrants and si
of the abdomen on the second or third day when the body is not immersed, m
not appear at all In the immersed body, however, on the fifth or sixth day,
comparable discoloration will appear in the head and neck. The generation of ga
in the immersed body may not be sufficient to cause the body to float until t
sixth to the tenth day. In warm water the body may float in 2 days; in cold wa
it may not float for several weeks.

Soon after immersion the skin of the hands and feet begins to wrinkle and m
become detached The hair loosens more quickly than do the nails of the han
and feet

The condition known as saponification may take place in an immersed bo
as well as in buried bodies or in those exposed to rain, sun and warmth In sapo
ification the affected fat becomes swollen, whitened and greatly stiffened and oft
constitutes the bulk of the tissue clinging to the bones after the skin and muscl
have gone

When the thoracic cavity of a drowned person is opened, the lungs bulge ou
ward and appear moderately congested, but sometimes are pale, owing to air an
water which have been trapped in the alveoli When the lungs are voluminous, re
and gray patches may be seen on the surfaces On section an edematous conditio
due to the presence of a copious, watery, frothy, blood-stained exudate, will b
observed This fluid is readily expressed on pressure of the cut surfaces or ma
exude spontaneously The presence of this fine, clear or, occasionally, blood-tinge
foamy or frothy fluid unmistakably points to death by acute pulmonary edema
by drowning

The stomach contains water, or liquid, corresponding to the drowning mediu
or to substances found in it

When putrefaction has become established, many of the signs which have bee
described are masked

The Heart and Blood in Fresh-Water Drowning and in Salt-Water Drownin
Swann, Brucer, Moore and Vezien found that there is abrupt and pronounce
hemodilution in drowning in fresh water as shown by rapid falls in plasma protei
hemoglobin, chloride and other constituents of the blood They found the convers
a strong hemoconcentration, in drowning in sea water Their data reveal that i
fresh-water drowning the blood may dilute to as much as twice its volume Con
versely, in sea-water drowning, nearly one third of the water of blood may b
removed These sudden alterations in the concentration of blood might be expecte
to have significant effects on the heart During sea-water drowning the heart ma
retain fair functional activity for nearly twice as long as in fresh-water drowning

METHODS OF ARTIFICIAL RESPIRATION (DROWNING) The methods for artifi
cial respiration are classified as manual and mechanical The term mechanica
according to Gordon, Famer, and Ivy indicates that some sort of apparatus o
device, even though only a board or stretcher, is used during the administration o
artificial respiration.

The application of a method of artificial respiration is a lifesaving measure to
those who have been submerged in water but in whom life still remains. The
methods of manual artificial respiration may be divided into four groups depending
on the manipulations used in the procedure. (1) The methods which give forced
expiration. These are termed push methods, the classic example of which is the
Schafer method of artificial respiration (2) The methods which give forced
inspiration. These are the pull methods, represented by the first-stage Silvester and
the hip lift manipulations. (3) The methods which combine the manipulations of
forced expiration and inspiration. These are termed push-and-pull methods, for
instance, the Nielsen, the Silvester and the modification of the Schafer method
known as the hip-lift Schafer method. (4) The mouth-to-mouth insufflation method.

This is more often used in resuscitation of children than of adults. Mouth-to-mouth insufflation is an ancient method of artificial respiration since it was possibly employed by Elisha in resuscitating the son of the Shunammite (II Kings, Chapter IV, Verse 34).

In recent years investigative work has been done to determine the relative efficacy of the various methods employed in artificial respiration. In 1951 Gordon, Sadov, Raymon and Ivy recommended for general use the Nielsen method. These investigators seem to believe, however, that the Schafer-Emerson-Ivy (hip lift-prone pressure) method was the most effective of all methods. Since 1951 various organizations, such as the American National Red Cross, have approved or adopted the Nielsen method

The preferable method of artificial respiration is determined by the circumstances under which it is to be employed and the experience and the physical condition of the operator For instance, on removal of a body from the water of a swollen stream to a brushy, muddy, slippery bank, by one who is alone and exhausted it is well for him to know the importance of placing the asphyxiated person in a position so that his head is somewhat lower than his thorax, face down, the forehead placed in the palm of the victim's hand as in the Nielsen method Despite exhaustion, the operator can usually muster enough strength intermittently to elevate the elbows and to push downward 10 to 20 times per minute on the lower back and ribs

The most important accomplishment to be obtained in resuscitation after immersion is removal of water from the lungs as rapidly as possible. As the water is removed from the lungs the space occupied by it is filled with air. Therefore, artificial respiration is immediately urgent

The Nielsen method (Fig. 19-1) of artificial respiration requires that the victim be placed in the prone position with the forehead resting in the palm of one hand which is resting on the other. Percussions with the fist are administered between the scapulae to force the tongue back into position The elbows are grasped and raised to cause active inspiration, they are then released, and pressure is exerted over both scapulae to produce active expiration The maneuver is performed rhythmically 10 to 20 times per minute. Undue pressure may fracture the ribs.



After Gordon Fainer and Ivy J.A.M.A., 144 1455, 1950

Fig 19-1 The Nielsen method of artificial respiration

The *Schafer (prone pressure) method* (Fig 19-2) is the simplest and for this reason it has been widely used as a method of artificial respiration The patient is placed in the prone position with arms extended and face to one side Pressure is exerted with the hands close together on the lower portion of the thorax. The pressure is rhythmically applied and relaxed at about the rate per minute of normal quiet respiration. The pressure on the thorax causes active expiration and passive inspiration as the result of elastic recoil of the lungs when the pressure is relaxed. The maneuver requires little

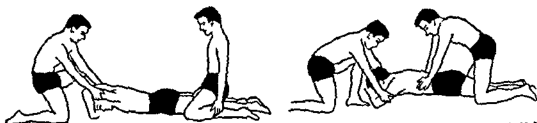
(Fig 19-3) requires that the patient be placed performs the prone pressure procedure of the Schafer method while another operator alternately raises the elbows or arms. The Drinker method thus eliminates the pressure exerted over the scapular area in the

Nielsen method and consequently avoids possible fractures of the ribs. At the same time it retains the well-known features of the Schafer method.



After Gordon, Fainer and Ivy J A M A 144 1455, 1950

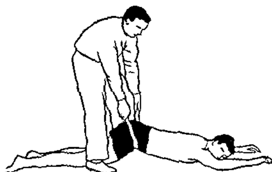
Fig 19-2 The Schafer (prone pressure) method of artificial respiration



After Gordon Fainer and Ivy, J A M A 144 1455, 1950

Fig 19-3 Schafer-Nielsen-Drinker method of artificial respiration

The *Emerson method* is performed by raising and lowering the hips with the patient in the prone position as in the Nielsen method Raising the hips several inches causes active inspiration because of descent of the inert diaphragm and hyperextension of the spinal column. Lowering of the hips results in passive expiration. Mechanical devices are available for executing this method A belt employed as shown in Figure 19-4 may be of great help.



After Gordon, Fainer and Ivy J A M A 144 1455, 1950

Fig. 19-4 Emerson method when belt is used for the hip-raising maneuver

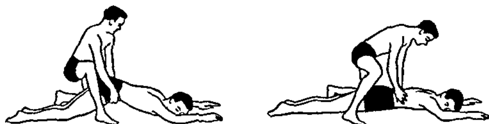
The *Schafer-Emerson-Ivy (hip lift-prone pressure) method* (Fig 19-5) is employed with the patient prone. This method alternates the lifting and lowering of the hips as in the Emerson method with pressure exerted on the lower part of the thorax as in the Schafer method Early muscular exhaustion of the operator may be avoided by the use of a piece of cloth, a shirt or a belt passed beneath the patient's hips, so that the lifting may be conducted by one or two persons while another carries on the prone-pressure maneuver. This method can be employed for a short interval in the treatment of acute paralytic poliomyelitis

Gordon, Fainer, and Ivy found that often the supine position results in respiratory obstruction. The "push" or "pull" methods alone do not ventilate. The manual methods [illegible] which the subject lies prone or supine and which utilize a "push-and-pull" principle [illegible] which [illegible] person [illegible] yield

method) is added [illegible] (Schafer-Emerson-Ivy method), it is as effective in restoring a "push-and-pull" method [illegible] Schafer-Nielsen-Drinker method. respiration as either the Nielsen method or the [illegible] (Fig 19-6), in order to reduce the fatigue

In the *hip roll-prone pressure method* [illegible] the victim is grasped at the distant hip and repeatedly is incident to lifting the hips, [illegible]

"rolled" onto and off the rescuer's knee. This can be accomplished alone or in conjunction with Schafer prone pressure.



After Gordon Fainer and Ivy, J.A.M.A., 144 1455, 1950

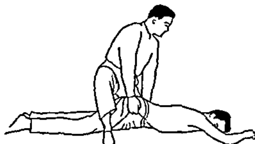
Fig 19-5 Schafer-Emerson-Ivy method of artificial respiration.

The simple method employed by Silvester (Fig 19-7) is not often used.

Mechanical Methods. In the *Eve (rocking) method* the patient is placed in the prone position and is rocked in a head-down and then feet-down position. Unlike the manual methods, the rocking method depends solely on the up-and-down motion of the diaphragm produced by the movements of the abdominal viscera during rocking

The *automatic intermittent positive pressure method* expands the chest by intermittently introducing air or a gas mixture under pressure (up to 20 cm of water or 14 7 mm of mercury) into the upper respiratory passages via a face mask A Burns valve may be used as a positive pressure device.

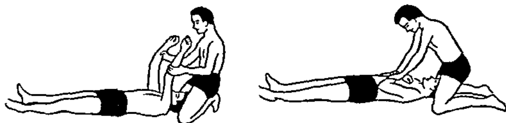
In the *alternating negative and positive pressure (suck and blow) method* a positive pressure of +14 mm. of mercury and a negative pressure of approximately −9 mm. of mercury via a face mask are applied rhythmically.



After Gordon, Fainer and Ivy, J.A M A, 144 1455, 1950

Fig 19-6 Modification of hip-lift method

Gordon, Fainer and Ivy concluded that except for the equipment of the anesthetist and the fire, police and rescue emergency crews, all mechanical devices must always be considered as adjuncts and not substitutes for the manual method, preferably of the "push-and-pull" type. The mechanical resuscitator operating at a maximal mask pressure of +14 mm of mercury is no more effective than a properly performed "push-and-pull" manual method On the other hand, the



After Gordon, Fainer and Ivy, J.A M A, 144 1455, 1950

Fig 19-7. Silvester method of artificial respiration.

properly employed mechanical resuscitator requires less skill than a properly executed "push-and-pull" manual method, is not fatiguing, and can furnish 100 per cent oxygen; herein lie the most important advantages of a good mechanical resuscitator There are other advantages, however. Since a resuscitator need be applied only once to a patient's face, it can be employed where physical manipulation of the body is impossible or would be harmful, as during major surgical procedures, for victims of accidents with extensive

burns, broken vertebrae, ribs or arms, for victims trapped under debris of excavations or overturned vehicles, and during transportation to a hospital. Some resuscitators signal when the airway is obstructed and provide an aspirator.

ASPHYXIA AND HANGING. Hanging is that form of death which is caused by suspension of the body by a line or rope which encircles the neck, the constricting force being the weight of the body. The proximate cause of death is asphyxia.

When the ligature is not tight, death may come slowly. The point of application of the force is an important factor not only in the time occupied in dying but also in the subsequent postmortem appearances. As the result of the constriction of the neck, entry of air to the lungs is hindered or prevented, the cerebral circulation is impeded and the phrenic and vagus nerves are compressed. Apart from implication of respiration a person may die from the effects of suspension on the circulation and from nerve injury. Pressure on the vagus nerves may cause cardiac inhibition and sudden death before asphyxial manifestations are established This possibility is always considered at the postmortem examination of bodies of persons found hanged.

As in other forms of death from asphyxia, the heart continues to beat for a few minutes after the cessation of respiration, and, therefore, artificial respiration on a suspended person may prove successful if the body is cut down within 5 or 6 minutes after the commencement of suspension After 5 minutes there is little chance of success in the re-establishment of breathing by any means

On examination of a body found suspended by the neck, when the ligature itself is not available for inspection, indications in the vicinity of a ligature mark, such as scratches or small bruises, may be suggestive of the nature of the ligature used. These marks may have been produced by a ligature or by the finger nails of the victim or those of an assailant in throttling, prior to suspension of the body to simulate suicide by hanging In doubtful cases, to eliminate the possibility of the body having been suspended after death, a piece of tissue from the ligature mark should be excised so that histologic examination may determine the presence or absence of vital reaction from trauma. Bruising associated with the ligature mark indicates either that the violence responsible was operative during life or that it was applied immediately after death while there was continuance of molecular life of the tissues

ASPHYXIA AND STRANGULATION Strangulation is that form of death caused by a constricting force applied around the neck by means of a ligature without suspension of the body. The constricting mark is usually found at a lower level on the neck than in hanging, but may be found at any level, and frequently direct pressure is exerted upon the larynx. The mark in some cases may be continuous around the neck; in others it may be invisible at some part of the neck.

Homicidal strangulation is common. It occasionally is associated with violation of a female victim

Under favorable circumstances, *asphyxia from any cause*, if life remains, may be relieved by institution of artificial respiration

Infant Deaths from Suffocation. At a conference on sudden death in infants which was held under the auspices of the Children's Bureau and the National Institutes of Health (November 30, 1949), Dr. Katherine Bain summed up the situation as follows:

Each year in the United States a large number of babies under 1 year of age die of what is classified as "accidental mechanical suffocation" The story behind the death is usually this: An infant, in apparent good health and usually between the ages of 2 and 5 months, is put to bed in a crib or baby buggy, or in bed with his parents Several hours later the infant is found dead Sometimes he is lying on his face; sometimes bedclothes are over his head Often in the excitement of the discovery the exact conditions are

unnoted The physician, the coroner or the medical examiner, confronted with such a death, is likely to assume that the baby has smothered. And without an autopsy, or at best after a sketchy one, he writes on the birth certificate that the baby's death was due to "accidental mechanical suffocation." The mother and father of a baby who has died in this way develop a great sense of guilt, which may disturb their lives for years But there is now abundant evidence that most of these deaths are not due to any external cause but may be the result of a sudden overwhelming infection with which a young baby is not able to cope. When a careful postmortem examination is made, including a microscopic study, evidence of infection is often found in the baby's respiratory tract, though sometimes elsewhere in his body, as in the membranes of the brain When a careful history is taken, information is often brought out concerning respiratory infection in the family, and there may be some indication that the baby himself had not been up to par.

Sudden Death in Status Lymphaticus. Status lymphaticus is regarded in the United States of America as a clinically recognizable entity consisting of a combination of hereditary constitutional anomalies, entering into which are certain peculiarities of configuration, with preservation or even hyperplasia of the thymus at an age when involution is to be expected, hyperplasia of the lymphoid cells in the spleen, intestine and elsewhere, changes in the distribution of hair, hypoplasia of the vascular system, developmental deficiencies in the genitalia, and visceral defects of uncertain occurrence and irregular distribution

In children who have expired suddenly with the physical attributes of status lymphaticus, the lymphoid tissues in various parts of the body reveal on postmortem examination myriads of necroses in the cells of the germinal follicles. These changes are believed to result in the release of sensitizing nucleoproteins. After the expiration of the anaphylactic incubation period the lymph nodes, according to this theory, are again subjected to the action of destructive substances which now serve to bring about further disintegration of nuclei, thus providing the requisite quantity of specific proteins to complete the sensitizing process.

Many do not believe that such an entity as status lymphaticus exists.

CHEMICAL AGENTS OF DISEASE

In industry and in everyday life a person may be subjected to exposure to injurious chemical agents and to their effects. In order to discuss the diseases caused by these chemical agents, some reference is made to their composition, manufacture and how contacts with them may be made.

A chemical may injure by contact with the skin, by inhalation, and by ingestion into the alimentary tract The injuries from chemical agents may be largely limited to the places of local contact On the other hand, the chemical may be absorbed from the skin, the lungs, or the stomach and intestines and may cause systemic disease after absorption.

From those suspected to be suffering from the ill effects of a poison a detailed account is obtained of precisely the work done, its relationship to chemicals and the possibility of having been exposed to poisonous materials An account is elicited of the habits of eating and drinking, and what has been eaten and drunk Inquiry is made in regard to accidents, medications, new household equipment, plumbing, new clothing, or the purchase of new cooking utensils, *ad infinitum*.

If the patient has been employed where there is the possible chance of exposure to the effects of chemicals, it should be recorded whether or not medical examinations were made (1) before beginning the work, (2) at regular intervals after being employed and (3) at the termination of employment or at the time of transfer from one job to another.

The pre-employment examinations in many of the industries are comprehensive and include a history, physical examination, roentgenologic examination of the

thorax, and laboratory examinations of the blood and urine. The results of these investigations are kept for future reference

After an employee has been selected *for a job, the frequency and thoroughness* of his physical examination depend on the hazards present. Each time an employee is transferred from one job to another, or when he is released from work, examination is made. The release examination is as comprehensive as the pre-employment examination.

At the time of examination at intervals during employment and at the time of discharge it is kept in mind that the common manifestations of being chronically affected by many different poisons are the same. These manifestations are easiness of fatigue, headache in one not accustomed to headaches, nausea, loss of appetite, sensation of fullness of the stomach, gas on the stomach, pain in the epigastrium, dizziness, precordial pain, pain or tingling of the extremities, and dyspnea on slight exertion.

The first signs of exposure to toxic chemicals are changes in pulse rate and in *diastolic blood pressure.* The blood pressure should be measured with the patient sitting, according to the recent recommendations of the Committee for Standardization of Blood Pressure Readings of the American Heart Association It is best to take measurements on both arms as well as to record the two levels of diastolic blood pressure

Acute exposure to toxic chemicals sufficient to cause a fall in diastolic and systolic blood pressures may lead to circulatory collapse. Collapse is due, in most instances, to a failure of the circulation to overcome the effects of gravity, so that insufficient blood is returned to the right side of the heart. If this condition is detected immediately, rest in the supine position, with the head lower than the legs, can restore normal circulation. If circulatory collapse is not detected, and the man falls, he may automatically reach the horizontal position and so restore circulation to normal; but, should he fall in a cramped position, sudden death may ensue

In the practice of medicine away from industry the possibilities of acute or *chronic poisoning are more remote than in industry,* and often a history of exposure to chemicals is absent or indefinite. Under these more adverse conditions, if poisoning is suspected, there are certain evidences in the history or on examination of the patient which will be diagnostically helpful

The *general appearance of the patient* is not characteristic of poisoning without a definite history of exposure to a noxious substance. Fear, anxiety, and a state of excitation are most commonly observed in those who have not been poisoned but who fear the presence of an impending disaster from disease or who may doubt their own ability to convince the physician of the validity of their complaints and to gain his agreement with their diagnosis of their ailments.

The Skin. *Changes in the color of the skin* consisting of pallor, or variations thereof, and cyanosis are most commonly due to systemic diseases Pallor, if due to *poisoning, is rarely present without other manifestations.* Pallor, however, may be present in acute poisoning by many substances, notable among them is the acute poisoning due to ergot, ether or lead

A cyanosis may result from bronchial spasm (constriction) or from an increased demand for oxygen Severe bronchial irritation may follow the inhalation of chlorine or ammonia gas and may prevent adequate breathing and thus create a need for oxygen as is observed in poisoning by dinitrophenol

Some poisons, su [illegible] and
prevent oxygenation, [illegible]
cause cyanosis, while [illegible]
from the combination of a foreign substance with the hemoglobin is [illegible]
poisoning by sulfides, and there is sulfhemoglobinemia. An example of poisoning causing a lividity of the skin is that of benzol.

An *artificially darkened skin* may be differentiated from a skin darkened by cyanosis by pressure on it with a glass slide. The artificially darkened skin will not blanch from pressure

An *excessive pink color of the skin* is most commonly observed in alkalosis from deep breathing due to hysteria It indicates the presence of an excessive amount of oxyhemoglobin and when due to poisoning, it may be caused by cyanides, atropine or carbon monoxide.

A *yellowish discoloration of the skin* is commonly due to excessive amounts of serum bilirubin—jaundice. When the discoloration is due to a poison, the common offending substances are picric acid, atabrine, and yellow dyes This yellow color is of a darker shade than the bronze coloring observed in poisoning by arsenic or arsenic compounds such as arsine

A *dry scaly skin* is present in many of the contact dermatitides (see Chapters 18 and 20) A *wet skin,* in the absence of a subsiding fever, may be occasioned by an increased activity of the sweat glands such as is observed from the effects of aspirin, insulin, and bites of snakes and spiders.

Fever. *Fever is the common manifestation* of the mechanisms of body defense from such a great variety of injuries that it may be misleading by its presence. It is well, however, to remember that an increased body temperature is frequently a manifestation of a poison Particularly important is the presence of fever in instances of poisoning by metals, the so-called metal fever. Chills and fever may occur after a poison has been given by mouth or intravenously (see Body Temperature, Chapter 22)

Nausea and Vomiting. Nausea, vomiting, anorexia, and abdominal pain are among the commonest symptoms of poisoning. The amount of abdominal pain present is usually indicative of the dosage of a poison or of whether or not the patient
[illegible] The presence of these symptoms, associ-
fear of impending death by the patient
onment in which the physician finds the victim of accidental poisoning if such has occurred in the patient's home. The next most frequent general observation of a victim of poisoning is to find the patient asleep in the midst of an apprehensive family.

The Mouth. Nausea, vomiting and abdominal pain arise from irritation, ulceration, and corrosions of the gastrointestinal tract. The examiner may help himself toward identifying the nature of a poison by observing the inflammation and edema of the lips which are present after contact with irritant materials. Likewise the oral cavity may be immediately affected from caustics, but its involvement more commonly is a secondary inflammatory stomatitis which is less immediately associated with acute poisoning The classic example of a stomatitis from poisoning is that known as salivation from the effects of calomel, a compound of mercury Other drugs and chemicals may invoke stomatitis, and many of them cause severe deep ulcerations of the gingivae

In the absence of stomatitis the mucous membranes of the mouth may be cyanotic from hypoxemia, or pink from carbon monoxide and cyanide. Yellow mucous membranes are caused by dyestuffs, picric acid, atabrine, chromates and, in the late stages of poisoning, from phenol On surfaces of the teeth there may be deposits of various nonmetallic or metallic substances such as carbon, copper, nickel, iron, mercury, lead and manganese These deposits are usually associated with a line along the gingival margins, for instance, the "lead line"

The changes in the mouth incident to poisons are greatly influenced by the amount of saliva present Therefore the effects of the noxious agent on the salivary [illegible]
ber of com-
or instance,

The secretions of the salivary glands are stimulated by physostigmine, prostigmine (neostigmine), pilocarpine, quinine, strychnine and iodides. The chemicals which stimulate these glands may give rise to inflammations in them. The chemicals which commonly originate inflammation of the salivary glands are iodides, lead, and arsenic. Often parotitis is originated by botulism.

The Esophagus and Stomach. The esophageal symptoms from immediate poisoning or following the ingestion of corrosives are not immediately distinct. They are overshadowed by the symptoms arising in the mouth and stomach The symptoms of esophagitis are described with the disorders of the esophagus (Chapter 13). Corrosive ulcers of the esophagus or the stomach may arise which may cause free perforation or become chronic indolent ulcerations.

Aside from the immediate irritative and corrosive effects of poisons when they reach the stomach, little can be said with certainty concerning the production of subacute or chronic gastritis of prolonged duration The immediate irritation of the stomach by foreign substances which provokes vomiting is a protective mechanism which saves many lives

The Intestines. Diarrhea, like vomiting, is a protective mechanism. Bloody dysentery may originate from injury to the mucous membranes of the intestines Metallic substances, such as compounds of antimony, arsenic, barium, bromine, copper, and mercury more commonly than other poisons cause diarrhea Many of the vegetable substances cause diarrhea, and some, a very severe diarrhea.

Constipation may originate from spasm of the intestine, particularly the colon, or from atony or paralysis Constipation arising from spasm of the bowel is difficult to interpret. Many times spasm of the colon is prolonged and severe from tension and anxiety, caused by the fear of an impending disaster. Constipation occurs immediately from the action of the alkaloids of opium Chronic constipation is characteristically present in poisoning from some of the metals, particularly from lead.

The Liver. Owing to the circulatory arrangement of the liver in association with the gastrointestinal tract, the liver is next in order to be affected by poisons being absorbed from the intestines Poisons received by the liver may be stored there or excreted through the liver in the bile The liver therefore is thoroughly exposed to noxious materials arriving from the intestines.

The liver is injured by chemicals and drugs by (1) idiosyncrasy, an individual peculiarity of metabolism which results in exceptional susceptibility; (2) cumulation, in which the effects of repeated small doses are identical with those of a single larger dose. This may be the result of direct chemical effect, of storage of the substance in the body with continuous injury, or of continued organic change as the result of scar formation after the drug has been eliminated; (3) nonallergic sensitivity, in which a usually harmless agent injures the liver because the organ has received some previous injury which lowers its resistance to any toxic substance; and (4) allergic sensitivity, in which previous exposure to the causative agent has produced sensitivity in certain susceptible persons, the average person not being sensitive to the drug despite the use of large doses

The subject of toxic hepatitis is considered in association with diseases of the hemic system (Chapter 12), diseases of the liver in Chapter 13, and in association with descriptions of the poisons which may injure the liver, in this chapter.

The Heart. The blood pressure is often affected secondarily from the effects of poison. Palpitation, pain in the chest, fainting spells, and circulatory collapse if present are often reflex in origin and not due to primary effects of poisoning. Auricular fibrillation may originate from poisoning by digitalis or quinine which ... occur from

cardial disease ... methemoglobinemia.

Respiration. Changes in respirations are very common manifestations of systemic disease or diseases of the body as a whole. The type of the respiratory response to a poison varies with the toxic substance, its action, its intensity, and the length of time during which the patient was exposed to it The rate, volume and vigor of the respiratory movements depend on the responsiveness of the medullary centers to the dissolved toxic agent, on the quantity of carbon dioxide or on disturbances of oxyhemoglobin concentrations, since they all may effect changes in the respiratory rate and in the blood pressure

The common initial respiratory response to a poison is an increase in the rate and depth of respiration as the result of hypoxia due to a replacement of oxygen in the inspired air by an inert gas such as carbon dioxide, nitrogen, nitrous oxide, helium, or methane or marsh gas, which may be present in old abandoned wells and caves There are many and varied poisonous compounds, such as the aromatic and aliphatic nitro compounds as well as the inorganic nitrites, which increase the rate and often the depth of the respiratory movements These nitro compounds cause a vasodilatation which may slow down the rate of blood flow and consequently decrease the supply of oxygen to the medullary centers. Similar disturbances of the medullary centers may be originated if a poison hampers the normal functioning of the oxidative enzymes. Such an effect occurs in cyanide and hydrogen sulfide poisoning

Slowed and difficult respiratory movements are usually indicative of acidosis. The acidosis, if due to a poison, may have originated in various ways; for instance, by a poison having displaced the normally present, easily dissociable amphoteric substances of the blood by more stable compounds and by engorgement of the lungs However, the more important toxicologic reasons for slow respiration ensue upon the accidental or intentional administration of chemicals which depress the activities of the central nervous system such as the alkaloids of opium, carbon tetrachloride, chloroform, barbiturates and hyoscyamine.

In poisoning by gases or easily volatile compounds such as ammonia, and the aromatic and aliphatic compounds, including gasoline, the odor on the breath may be the same as that of the toxic agent

The mucous membrane of the upper part of the respiratory tract may be irritated by the inhalation of either gaseous or particulate solid matter, and rhinitis and coryza may result Prolonged irritation of the nasal mucous membrane may cause hypertrophy and increased nasal secretions Epistaxis may be incident to such a condition of the nasal membranes Perforation of the nasal septum occurs in exposures to arsenic, copper, zinc, and chromic acid Irritating gases may induce edema of the glottis, while the accidental aspiration of caustic alkalies or acids may cause corrosion of the glottis. The same kind of irritants as those which produce edema and corrosion of the glottis may extend these processes into the larynx and down the trachea to the bronchi Irritation of the air passages from toxic substances may become infected, and thus pneumonitis may ensue Often, however, a pneumonia occurs as the result of aspiration of saliva or vomitus while the patient is unconscious from anesthetization or from other toxic action of the poison

Whenever the lower part of the respiratory system is severely injured from direct action by a toxic substance, pulmonary edema may ensue The edema may not develop until some time after the acute manifestations of the injury have subsided. In those injuries severe enough to originate pulmonary edema directly or as an allergic manifestation, pulmonary hemorrhages may be observed

Pulmonary hemorrhages may occur as a part of the acute injury by gases or they may come on late. All pulmonary hemorrhages from irritating substances are preceded by hard spasmodic coughs

The critical and dangerous respiratory manifestations of injury from toxic or irritating substances are pulmonary hemorrhages, edema, and sudden respiratory

arrest. A sudden respiratory arrest occurs as the result of overstimulation of the medullary centers Sudden overstimulation may result from severe irritation of the respiratory passages, as when flames of fire are inhaled; also an anoxia or a paralysis of the respiratory muscles from the administration of curare.

The Kidneys and Bladder. A poison, once in the body, may be excreted by any of the excretory systems, for instance, the integumentary, the respiratory, the digestive, or the urinary system Aside from the injury which may be sustained by the kidneys, the toxic material may injure the ureters or bladder.

The kidneys have the main responsibility for excretion of those noxious materials which are absorbed into the blood The blood renders many poisons innoxious to the body and to the kidneys. The kidneys may be injured directly by attempting, or by accomplishing, the task of excretion of poisons They may suffer indirectly from changes and variations of the blood pressure secondary to the effects of poisons.

Renal changes of sufficient degree to be diagnosable are manifested as either a nephrosis or a nephritis.

In the exit of urine containing poisons excreted from the kidneys the bladder may be affected and stranguria may ensue. Common examples of poisons causing stranguria are turpentine, toluidine, santonin, ergot, strychnine, and overdoses of morphine.

Urinary incontinence is incident to paralysis of the sphincters of the bladder and is common in overdoses of barbiturates, bromide, and sulfonal

The Endocrine Glands. Measurable effects of poisoning can rarely be assigned as the cause of dysfunction of the endocrine glands. In former times there were drugs offered which were thought to have the power of increasing the libido The libido if affected at all by a poison is first increased and then decreased. Decreased libido is common in various chronic poisonings just as it is common in all debilitating diseases.

The thyroid gland and the adrenal glands are rarely injured by poisons Lead, mercury and carbon monoxide may reduce thyroid functions The prolonged use of *iodides may injure the thyroid gland The adrenal glands may be injured by various* substances, but little is known about such injuries.

The effects of poisons on parturition are most commonly directly associated with injury to the fetus, with or without subsequent abortion It is much commoner to observe systemic poisoning from the use of a drug with the intention of causing abortion than of taking the life of the mother Abortion may be caused by poisoning with substances such as lead, arsenic, mercury, and phosphorus It is more commonly caused by organic substances such as ergot, quinine, nitrobenzene, turpentine, carbon tetrachloride and benzene

The Muscles. The muscles may be affected by direct action of a poison or they may be affected indirectly through the nervous system or circulatory disease A common example of the direct action of a poison causing paralysis is that of curare, while strychnine causes hypertonicity of the muscles with its central action is limited to the spinal cord.

Flaccid paralysis of the muscles follows certain chronic poisonings by both metallic and nonmetallic substances Common examples of metallic substances causing flaccid paralysis are arsenic, lead, and mercury. This paralysis is the result of peripheral neuritis Choreiform movements performed by the muscles originate from injury of the basal ganglia *Tremors usually characterized by rapid movements* of muscle groups of the hands and head are, as a rule, of hereditary origin and not due to a poison. Ataxia is a common muscular disturbance in poisoning, particularly by the alcohols

Convulsions often arise as a part of a convulsive state such as idiopathic epilepsy, and the apprehension in regard to having been poisoned intentionally or accidentally may increase the number of convulsions if a convulsive state is present. If a

convulsion arises from the action of a poison, there is nothing characteristic about it. Such fits occur as clonic convulsions and tonic convulsions of the musculature. The muscular convulsive response originates in the central nervous system or from the destruction of enzymes of the muscles. Stimulation of certain nerve centers with ensuing convulsions may be due to asphyxia, to circulatory disturbances, or to the formation of toxic substances in the body fluids

The Nervous System. The manifestations of the action of a poison on the central nervous system are central and peripheral. Variations in these manifestations are dependent on the susceptibility of the nervous system to injury and on its ability through anxiety, fear and apprehension to feign injury.

The manifestations of injury to the central nervous system may be headache, restlessness, confusion, disorientation, delirium, excitement, irritability, insomnia, fatigue, lassitude, somnolence, stupor, unconsciousness and coma. Hallucinations, catatonia, psychosis, mental deterioration and dementia all may occur in various sorts of poisoning, but these cannot be the assigned effects of poisoning until proved.

Pain in the extremities in the course of peripheral nerves is a most important manifestation of chronic poisoning of various sorts If the pain is associated with both sensory changes and motor disturbances, a peripheral nerve is affected. Peripheral neuritis may be accompanied by degrees of myalgia and arthralgia. Notable among the poisons causing peripheral neuritis are lead, arsenic, mercury and thallium Other important causes for peripheral neuritis are benzene, the monoxide and disulfide of carbon, oil of chenopodium, emetine, penicillin, and the sulfonamides

Vision and Hearing. The eyelids and the conjunctivae are frequently injured by poisonous or corrosive substances Von Oettingen lists 120 substances which have caused conjunctivitis, and no doubt this list could be greatly lengthened. Many of these and other substances may cause severe damage to the external structures of the eye by chemosis and corrosion

On contact of an irritant with the external structures of the eye, blepharospasm, lacrimation, and often photophobia ensue

In poisoning which acts through the central nervous system, but on rare occasions on the ocular nerves to the ocular muscles, the function of the oculomotor muscles may be impaired and be manifested by weakness of these muscles and the resulting abnormal position of the eyeball For instance, there may be exophthalmos, strabismus and nystagmus

Pupillary disturbance consisting of mydriasis alone or associated with rigidity is often the result of severe pain from any cause.

Common poisons which cause dilatation of the pupil are atropine, cocaine, ergot, insulin, and procaine The common drugs or poisons causing miosis or small pupils are caffeine, morphine, physostigmine, pilocarpine and chloroform.

Visual disturbances from poisoning may exist in all degrees from impaired vision, double vision, restriction of the visual field, disturbances in color vision, and yellow vision, to complete blindness The common poisons which may cause double vision are digitalis, ergot, insulin, morphine, quinine and ethanol (alcoholic beverages) The visual field is restricted by atropine, caffeine, epinephrine, ergot, morphine, quinine, salicylates and chloroform Disturbances in color vision are caused by barbiturates, digitalis, bromides, methyl alcohol (wood alcohol), quinine, salicylates and mercury (calomel) The common causes for yellow vision are digitalis, amyl nitrite, atropine, wood alcohol, and particularly santonin, when administered as a vermifuge

Poisons may injure both parts of the eighth cranial nerve. Defects in hearing, ranging from impairment to deafness, may follow poisoning from aspirin, atropine, quinine, streptomycin, cortisone, cocaine, the oxides and sulfides of carbon, and benzene. Vestibular disturbances may be caused by wood alcohol and amyl alcohol,

atropine, codeine, digitalis, kerosene, mercury, nitrites, opium, phenol, prostigmine, ethyl alcohol, lead, sulfonamides, thymol and many others.

ORGANIC COMPOUNDS

Benzene (Lethal Dose ⅓ Ounce to 1 Ounce). The symptoms of acute benzene poisoning are headache, dizziness and a feeling of intoxication.

In *acute benzene (benzol) poisoning* the most characteristic change is dark red blood which is very slow to clot but which does not show hemolysis. Hemorrhages, usually punctate, are found in the lungs and pancreas and in the gastric and intestinal mucous membranes. The abdominal organs are congested and there are *many bright red spots on the skin*

Treatment for acute poisoning consists of gastric lavage, followed by the administration of milk, tea and, if necessary, heart stimulants

Chronic benzene poisoning is more frequent, more important and more difficult to diagnose and treat than the acute form

When benzene vapors enter the body in the acute poisoning, about one third is absorbed in the blood Of this absorbed benzene some is oxidized to phenol and diphenols such as catechols and hydroquinone and eliminated as such. More of the benzene is eliminated as esters of sulfuric and glycuronic acids than is oxidized. In chronic poisoning more of the benzene is absorbed by the blood and is fixed in the bone marrow, fatty tissue, and liver.

There is individual but variable susceptibility to benzol poisoning. Also, there is an individual variation in the time required for symptoms of the poisoning to develop. The anemia may be discovered in from a few weeks to many years after exposure

The tendency of men to react with hyperplasia of the bone marrow, and of women to react with aplasia, suggests that women are more susceptible to benzene than are men

The influence of benzene on the course of infections reveals a lack of response on the part of the patient to infection Severe lesions of the mouth, such as Vincent's angina, are the most frequent manifestation of this action of benzene. Osteomyelitis of the lower jaw and gangrenous stomatitis may ensue.

The symptoms of chronic benzene poisoning are progressive weakness, malaise and fatigue. Then oozing of blood from the gums, throat, and nose occurs, and petechial hemorrhages from the stomach, intestines, and uterus ensue There may be chills, fever, delirium, heart failure with pulmonary edema, or toxemia following suppurative lesions in the throat, and death.

In benzol poisoning the results of a general examination by physical means are normal or are in accordance with the symptoms just outlined. *The characteristic* blood findings of severe poisoning are leukopenia, thrombocytopenia, and a high-grade anemia As the anemia develops in severe poisoning, there are macrocytosis, thrombocytopenia and leukopenia Leukopenia may develop first if it is present at all. Other manifestations of benzol poisoning are eosinophilia, immature elements of marrow in the circulating blood, and evidence of increased destruction of blood. The serum bilirubin values may be increased

Erythropenia sometimes is present to the point at which there are no young erythrocytes in the circulating blood Leukopenia may advance to the stage in which not only is the number of polymorphonuclear cells low but there is an absence of myelocytes, myeloblasts, and lymphoblasts The platelets are decreased, *sometimes to very* low levels Coagulation of the blood is decreased in time, with no retraction of the clot ensuing on standing.

Typically, the erythrocytes should present a perfectly normal appearance

Of great aid in the diagnosis of early benzene poisoning is the urinary test devised by Schrenk, Pearce and Yant of the Bureau of Mines They found uniformly

that an early sign of benzene poisoning is a decrease in the proportion of inorganic sulfates to total sulfates, this decrease being marked in accordance with the severity of the intoxication. The same decrease may be present in the urine of benzene workers.

Normally the inorganic sulfates make up 85 to 95 per cent, the organic, ethereal or conjugated, 5 to 15 per cent, but in cases of benzene absorption the phenolic products that are formed take up the sulfur, and the result is an increase in the conjugated sulfates which reverses the foregoing proportions. The decrease occurs rapidly on exposure to benzene and well in advance of leukopenia or anemia or other evidence of injury.

Derivatives of Benzene. The derivatives of the benzene ring are numerous and it is not always possible to predict, from the chemical composition of the simpler members of the group, what the physiologic action probably will be.

A chief use of *phenol* (hydroxybenzene) is the production of plastics, especially bakelite, for which it is combined with formaldehyde. Complaints of disagreeable effects in the making and use of bakelite are usually referred to the formaldehyde. Severe burns may be caused by phenol (carbolic acid) or by cresol. Phenol is readily absorbed through the skin Extensive burns of the skin by picric acid (trinitrophenol) may cause collapse and death.

Dinitrophenol 1-2-4, or *alpha-dinitrophenol*, is a powerful stimulant to metabolism This excessive oxidation affects metabolism and nutrition and damages hepatic and renal cells The use of alpha-dinitrophenol for the treatment of obesity may cause serious poisoning with symptoms such as fever, profuse sweating, and restlessness, associated with agranulocytosis, polyneuritis, rapidly developing cataract, blindness, and dermatitis exfoliativa

Trinitrophenol (picric acid) on the skin results in a dermatitis, sometimes severe, abdominal cramps, vomiting, and diarrhea.

Tricresyl phosphate is used as a plasticizer in the plastics industry. Tricresyl phosphate may be present in the alcoholic drink Jamaica ginger. Ingestion of Jamaica ginger may be followed by "jake paralysis" in which there are bilateral drop foot and wristdrop as the result of degeneration of peripheral nerves and corresponding anterior horn cells. A similar condition may arise from the use of an abortifacient, apiol, adulterated with *tri-ortho-cresyl phosphate* Soya bean oil used for salads and cooking has been known to be contaminated with tri-ortho-cresyl phosphate, the use of which causes a lower motor neuron paralysis.

Diphenyl is two benzene rings linked together. *Chlorinated diphenyls* are toxic. The *diphenylamine* and *para-amino-diphenyl* have the toxic action characteristic of amido compounds and are absorbed chiefly through the skin *Tetryl* or *trinitrophenylmethylnitramine* causes a dermatosis which is the principal toxic disturbance if not the only form of poisoning present in those who handle tetryl products.

Pure *chlorbenzene* produces systemic poisoning with methemoglobinemia and the resulting oxygen starvation *Paradichlorbenzene* is a constituent of antimoth mixtures and insecticides and often gives rise to dermatitis Nitrochlor compounds are irritating to the skin *Nitrochlorobenzene* is toxic and first causes anoxemia, flushed face, pressure in the head which increases to a violent throbbing headache, with dizziness, weakness and perhaps dyspnea. In severe poisoning the lips, tongue, and ears are deeply cyanosed Nausea, sometimes vomiting, a complaint of cramps in the abdomen, a staggering gait, and extreme weakness are present Such attacks always occur several hours after exposure The livid color persists for several days after acute poisoning, and in chronic poisoning it is plainly obvious all the time. The livid color, breathlessness on exertion and attacks of vertigo and gastric upset simulate cardiac disease. These symptoms may cause a serious disability with slow recovery.

Dinitrobenzene passes rapidly through the skin and also is inhaled as vapor.

If a sufficient dose is obtained, death may ensue in 1 to 2 days. In chronic poisoning there is a severe form of anemia, the skin is dusky yellow, and the conjunctivae are jaundiced, the muscles waste, sensation is dulled, and paresis of the hands with paresthesias, hyperesthesia and defects of vision are present. The effect on the bone marrow is at first stimulation of active erythrocyte production, as shown by polycythemia and then inactivity of the marrow follows. There are evidences of effort at regeneration: stippled erythrocytes, polychromatophilia, nucleated forms, variation in size of cells, and diminished platelets and lymphocytosis.

Trinitrotoluene ($C_6H_2(NO_2)_3CH_3$), TNT, is capable of causing dermatitis Workers with TNT and aniline dyes have an increased susceptibility to alcohol A small amount (a single drink) of whiskey may be enough to cause acute intoxication Anilinism is the term used to designate poisoning from aniline fumes

Paranitraniline is used with beta naphthol for the production on fabric of a bright red dye called parared. This, like other aniline compounds, may cause dermatitis, and even fatal sytemic poisoning Instances of the latter are rare. When they do occur, they result from exposure of a large part of the body to the dust of the dry compounds. A few hours after exposure there is unconsciousness, and death may ensue Often recovery may be hastened by intravenous injections of methylene blue

Paraphenylendiamine (ursol) is a dye for fur and felt. Poisoning from paraphenylendiamine is comparatively common among those who wear fur dyed with this compound The dye causes a severe dermatitis and, in some, bronchial asthma, an allergic reaction which is explained by the acute edema of the bronchial tubes. The patch skin test is often diagnostic.

Ethanolaniline or *2-anilinethanol* (phenylethanol amine) is toxic in the same way as the compounds of the aniline group. It produces methemoglobinemia The symptoms are headache, dizziness, pains in the muscles of the legs, breathlessness, and cyanosis. The blood is a deep brownish blue and the urine is dark. The cyanosis subsides after 24 hours

Toluene and Xylene. Toluene is methyl benzene, xylene is dimethyl benzene Owing to the inclusion of the methyl radical in the molecule, both toxicity and volatility are reduced Commercial toluene and xylene are very likely to contain benzene If the benzene content is high, benzene poisoning may ensue from handling

The affinity of benzene and toluene for the lipase substances present in the cells of the central nervous system attracts the ill effects of these chemicals on this system The poisoning characteristically causes inebriation, narcosis and psychosis Headache, vertigo, nausea, fatigue and giddiness are the predominant complaints, and disturbance of equilibrium (with a positive Romberg sign), ataxia, paresthesia and staggering gait the chief manifestations Psychotic disturbances manifest themselves in restlessness, disorientation, loss of memory, fugues, hallucinations and irritability, culminating in loss of consciousness. The wearing of respirators should be rigidly enforced in those working for even a short period in heavy concentrations of benzene and toluene.

In either toluene or xylene poisoning, there may be a decrease in the number of erythrocytes after exposure to high concentrations, a proportionately lowered hemoglobin, marked leukocytosis, and a considerable fluctuation in the proportion of lymphocytes to granulocytes

Toluene does not cause a reduction in the ratio of inorganic sulfates to the ethereal sulfates excreted in the urine, it does cause an increased excretion of hippuric acid which is roughly parallel to the intensity of the exposure.

Derivatives of Toluene and Xylene. The *toluidines* are amino derivatives of toluene. These compounds are irritating to the urinary system, causing strangury and hematuria. The para-toluidine seems to be more toxic than ortho-toluidine, despite the fact that it is a solid, while ortho-toluidine is a liquid.

Trinitrotoluene poisoning causes breathlessness on exertion, dizziness on stooping over, persistent headache, fatigue, anorexia, bad taste, and nausea in the morning. The conjunctivae smart and secrete excessively. The nose and throat burn and often there is nosebleed. The urine becomes clear brown in color. The Webster reaction of the urine is positive. This color test reveals a reduction product of trinitrotoluene which is proof only of absorption and not of poisoning, whereas the presence of *porphyrinuria* may indicate intoxication. In all instances of severe poisoning, the liver, the bone marrow and the vascular endothelium are affected simultaneously. The symptoms may be those of acute toxic hepatitis, if the liver is most involved, or of aplastic anemia or of acute toxic purpura.

Naphthalene fumes may cause headache, nausea, and vomiting and if hot and concentrated, injury to the cornea and bilateral optic neuritis *Tetralin*, tetrahydronaphthalene, is used as a degreaser and as a substitute for turpentine in paint or floor finishes The vapors are irritating to the mucous membranes and conjunctivae and also cause nausea, headache, and stupor. A dark, olive green coloration of the urine is present The color is attributed to the hydrolysis of tetralin, which is excreted as conjugated glycuronic acid.

The *naphthols* vary in solubility and isomeric arrangements. Beta naphthols give rise to skin irritation, cyanosis, frequent micturition and evidence of irritation of the bladder. Nitronaphthol (Marius yellow) is likewise a skin irritant. Alpha naphthol is harmless

The simpler compounds of chlorinated naphthalenes are commercially known as *halowax*. They are a cause of severe forms of acne, cable itch or blackhead itch

For many years the only recognized industrial injury from the use of halowax was a form of acne which differed from the ordinary form because itching was present The men called it blackhead itch and it appeared on the exposed skin It was often severe in type and secondary infections sometimes caused permanent scars. Vapors condensing on the skin act more quickly than does direct contact, and the melting temperature is around 240 to 260 F (115 5 to 126.6 C) at which point vapors are given off

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cally by jaundic [illegible]
are sufficient tc [illegible]
of the scleras Jaundice with anorexia, nausea, and severe abdominal pains ensue.

The Aniline Dyes. The aniline dyes are harmless. Dermatoses that sometimes affect dyemakers and dyers should be attributed to overharsh methods of cleaning the hands Cicatricial shrinkage of the conjunctivae of dye workers may occur.

Petroleum. The distillates of petroleum such as gasoline, naphtha, petroleum ether, and benzine and dry-cleaning fluids (Stoddard's solvent) have an acute anesthetic action Exposure to the fumes of these volatile solvent substances results in headache, blurred vision, dizziness, mental confusion, nausea, abdominal pain and, in extreme cases, loss of consciousness. These symptoms pass off promptly when fresh air is breathed, though occasionally there is a temporary exacerbation on coming into the open air. Massive doses result in sudden collapse, coma, and death.

Gasoline. Gasoline is a mixture of petroleum hydrocarbons having a distillation range of from less than 100 to about 400 F (204 C). Its composition in general comprises naphthenes, paraffins, aromatics and olefins All straight-run gasolines contain naphthene hydrocarbons. Straight-run gasoline made from petroleum pro- [illegible]

[illegible] at the filling station can be a possible source of poisoning The other sources of poisoning are the added constituents such as tetraethyl lead

Gasoline intoxication, as emphasized by Machle, occurs outside the petroleum industry when there is substitution of gasoline for solvents. Severe chronic gasoline poisoning has occurred in dry-cleaning plants; the pressing of clothes still damp with gasoline is dangerous because high temperatures volatilize the more toxic, heavier fractions, which are inhaled, and the toxicity is said to be likewise increased Cutaneous absorption is an insignificant means of absorption.

Gasoline is sometimes ingested accidentally, usually by children but also by motorists attempting to siphon it from tanks. The single oral dose usually fatal to man is approximately 7.5 gm per kilogram of body weight but death has been caused by a total dose as little as 10 gm., and recovery has followed the ingestion of 250 gm This divergence is due in part to the variability both in absorption and in the chemical composition of the gasoline It is absorbed most rapidly if it contains a high concentration of benzene and other aromatic hydrocarbons. The time interval between the ingestion of the gasoline and the occurrence of emesis and the possibility of aspiration are also of great toxicologic importance, since these factors influence the effective dose retained Individual susceptibility and the presence of food and fats in the stomach, tending to delay absorption, are factors in delaying or reducing poisoning

If the concentration of gasoline vapor in air is high, absorption through the lungs may be extremely rapid and symptoms may appear after a few minutes of exposure There is no agreement as to the amounts of volatile gasoline necessary to cause intoxication Susceptible persons may show symptoms after short exposures.

There are no characteristic general morbid anatomic changes incident to acute poisoning by gasoline The lungs are hyperemic There are petechial hemorrhages, subpleural extravasations and, in some instances, gross pulmonary hemorrhages Pleural effusion may be present Some degree of pneumonitis is usually present, especially if the gasoline has been ingested and aspiration has occurred, or as the result of its excretion by the lungs

Hemorrhages in the liver, kidneys and spleen and hemorrhages into the serous cavities are common The liver may be enlarged and contain cloudy swelling, and there may be fatty changes In the kidneys, edema may be present The proximal convoluted tubules are injured and the glomeruli contain lipid degenerative changes.

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In chronic poisoning the anatomic changes are neither pronounced nor specific.

SYMPTOMS *Acute Intoxication* On exposure to very high concentrations of gasoline vapor in air, the highly susceptible victim falls to the ground in a comatose state and may die at once or within a few hours without regaining consciousness In a less susceptible person the onset of coma may be less rapid and the acute anesthetic action of the gasoline may cause initial symptoms like those of acute alcoholic intoxication, a brief period of in-co-ordination, restlessness and great excitement, with combativeness and abusiveness, mental confusion, disorientation, ataxia and possibly disturbances of speech and of swallowing. Delirium and finally coma ensue.

Unsaturated hydrocarbons, particularly the aromatic series, cause convulsions, tremors and motor disturbance Meningismus and epileptiform fits may continue for some time after recovery from the coma

EXAMINATION On examination evidence of the symptomatic manifestations may be observed. The skin may be moist and cyanotic. Coma often is present The pulse is enfeebled and rapid in the early stages of coma; it is often full in the presence of considerable motor unrest. Bradycardia, however, may be present. The pulse returns slowly to normal with recovery The temperature is usually subnormal but a rise in temperature may occur and in very sick patients and in terminal states it has reached 10o F (about 41 C). Respirations are usually shallow, rapid, and irregular. Sudden apnea may occur.

In quiet coma the superficial and deep reflexes are weak or absent. In the

presence of jactitation, meningismus and convulsions the reflexes may be greatly increased and plantar extension may be obtained. The pupils are dilated, often fixed, and may be unequal. Conjugate deviation and strabismus are frequent. Vomiting and singultus sometimes are observed during coma and may persist.

Subacute Intoxication Under most conditions of exposure in the ranges that cause subacute poisoning, the concentrations of volatile gasoline vary widely within wide limits. Individual susceptibility seems to be an important etiologic factor

If sickness has occurred as the result of ingestion, with no aspiration of the gasoline, symptoms develop more slowly than in poisoning by inhalation. There are various premonitory symptoms headache, usually described simply as a feeling of pressure over the head, blurred vision, vertigo, ataxia, tinnitus, nausea and anorexia, weakness and in some cases general abdominal pain. With these symptoms there develops a state of intoxication like that produced by alcohol, known as naphtha jag The sensation may be pleasurable and persons have been known to inhale gasoline vapors intentionally

Chronic Intoxication. This term is applied to poisoning which results from exposure to low concentrations of gasoline vapor for long periods of time.

The first symptoms to appear in chronic intoxication are those of a general nature and closely resemble psychasthenic and neurasthenic manifestations They are followed by muscular weakness and cramps, listlessness and a feeling of fatigue, and loss of body weight Hayhurst's patients slowly lost from 10 to 60 per cent of their body weight Irritative properties of the vapor usually cause conjunctivitis with lacrimation and cough with expectoration. Pulmonary hemorrhage has been reported but is uncommon When pulmonary hemorrhage occurs causes other than gasoline fumes should be found

Symptoms due to the effect of chronic intoxication on the central nervous system are mental confusion, loss of memory, a sense of impaired mental faculties, depression, irritability and nervousness

Indigestion, anorexia, nausea, but rarely vomiting, may be complaints Generalized abdominal pain is frequent and there may be either constipation or diarrhea.

There is often evident loss of body weight These patients often present physical appearances and behavior comparable to those observed in persons who have chronic alcoholism.

The specific effect of gasoline, or benzene, on the blood seems to be present only in chronic intoxication In cases of chronic gasoline poisoning some degree of anemia is usual. Hemoglobin may vary from 60 to 90 per cent, with 3,000,000 to 4,000,000 erythocytes per cubic millimeter The number of leukocytes is little changed, usually slightly increased In those cases in which leukopenia has been reported there has usually been exposure to gasoline of high benzene content Thrombopenia, purpura and epistaxis may also occur

Chemical changes in the blood are not significant

Albuminuria caused by gasoline poisoning occurs in some cases and usually appears 3 or 4 days after exposure

The commonest complications of gasoline poisoning are peripheral neuritis, impairment of memory, dullness of intellect, paresthesias in the extremities, cranial nerve palsies, retrobulbar neuritis and epileptiform fits. The neuritis and paresthesia do not usually persist, in some, however, severe spinal cord or neuritic symptoms have persisted.

DIAGNOSIS In acute poisoning there is a history of exposure or ingestion, and the odor of gasoline on the clothes and skin If poisoning has been by ingestion, both vomitus and washings from lavage will have the odor of gasoline. The odor will also be detected in the expired air for hours if exposure has been to high concentrations.

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EXAMINATION. The distinctive odor of methyl alcohol or acetone is detected on the breath The pupils are dilated and sluggish in response to light in serious poisoning The conjunctivae are injected, and there is photophobia. There is reduction of central vision, developing 24 hours after ingestion. This is usually in the form of a negative central scotoma of the relative type. However, the scotomas may be anywhere in the visual fields. Night blindness, color impairment and yellow vision may occur.

The fundi may show generalized hyperemia The disks are hyperemic and the borders blurred owing to papillitis Secondary optic atrophy may occur in patients whose vision improved for four to six weeks

There are varying degrees of acetonuria. The levels of methanol in the blood may reach 40 to 50 mg. per 100 ml. and still recovery may ensue.

The pathologic changes in the eye are attributed to an optic neuritis. As the initial inflammation subsides, there is an improvement of vision which lasts until the scar tissue contracts, and atrophy of the optic nerve and permanent blindness ensue.

Combating the intense acidosis is the most important single feature of therapy. In severe poisoning 250 ml. of a 5 per cent solution of sodium bicarbonate can be administered intravenously and then continued measures to combat the acidosis may be used if necessary.

The diagnosis of methyl alcohol intoxication can be surmised from the evidence obtained from the history and the examination. Identification of methyl alcohol requires the services of the chemist.

Ethyl Alcohol. Ethyl alcohol (CH_3CH_2OH) has an *irritant action* owing to the partial precipitation of the proteins of the cells and to its dehydrating property.

[illegible]

unprotected surfaces the irritant action is much greater, and the application is attended with pain and smarting. In the mouth strong alcohol produces a burning, unpleasant sensation which passes to the throat and stomach when it is swallowed, and if the concentrated vapor is inhaled, it causes irritation and reflex closure of the glottis and cough or strangling.

Alcohol is absorbed rapidly, about 20 per cent of that ingested being taken up in the stomach and 80 per cent in the small intestine. The rate of absorption varies with the concentration, strong alcohol appearing more quickly in the blood than does the same amount in greater dilution, food delays the absorption when taken at the same time, especially if it contains fat The concentration of alcohol in the blood reaches its maximum about 2 hours after the alcohol is swallowed, and then the level falls slowly, the amount in the blood being determined by the balance between that which is being absorbed and the amount undergoing oxidation and excretion The course of intoxication follows the curve of the concentration in the blood fairly closely.

The most constant *pathologic changes* are severe meningeal and cerebral congestion, pulmonary edema, acute gastritis, visceral congestion and acute pancreatic necrosis Most of these changes are found in other conditions, especially those characterized by anoxemia Postmortem determinations of blood, urine and tissue alcohol are of diagnostic value only when death has taken place within a few hours after the onset of the alcoholic coma Acute alcoholism should be suspected in all cases of suicide, homicide, accident, trauma and poisoning and as a complicating or precipitating factor in other medical or surgical fatalities.

The *effects* of alcohol differ in different persons as well as in a given person at different times When drinking is indulged in in company, the stage of excitement is a common phenomenon, but if alcohol is taken in solitude, the excitement does not occur.

In small quantities, alcohol produces a feeling of well-being and good fellowship

Gasoline poisoning occurring in a room where gasoline combustion engines are operating may be confused with coma and convulsions from carbon monoxide intoxication. The color of the skin and mucous membranes and the finding of carbon monoxide hemoglobin in the blood will serve to identify the poisoning of carbon monoxide. In most cases of acute intoxication there is recovery without serious after-effects Severe sequelae are uncommon. It is to be emphasized that most of those who have gasoline poisoning or intoxication, in either the acute or chronic forms, recover completely. The manifestations which have been alleged to be the result of complications and which persist can rarely be proved to be due to gasoline *intoxication.*

Alcohols. The common alcohols, methyl, ethyl, isopropyl, butyl and amyl, increase in toxicity as the series becomes chemically more complex from methyl alcohol.

The acute effects of the alcohols, *methyl* and *ethyl,* do not differ except that the duration of intoxication with methyl alcohol is more prolonged than with ethyl alcohol. Ethyl alcohol is rapidly oxidized to carbon dioxide and water, which are disposed of quickly, whereas methyl alcohol is difficult to excrete and it is by this property that it is rendered so poisonous when ingested.

Methyl Alcohol. Methyl alcohol (CH_3OH) is properly known as methanol, and more commonly is called wood alcohol. It is an important industrial solvent and the major ingredient of many inexpensive antifreeze preparations

Acute or chronic poisoning may be produced by ingestion, cutaneous absorption or inhalation Atmospheric concentrations of 0 2 per cent may cause systemic complaints. The erroneous use of methyl for ethyl alcohol as a skin rub, or its criminal incorporation in cheap hair tonics or hand lotions, may produce poisoning Most commonly, however, intoxication occurs after using it for a spiritous beverage There is extreme variability in individual tolerance to this agent, but permanent blindness has been reported after ingestion of as little as 4 ml and death has occurred after drinking 30 ml.

One third of the assimilated dose of methanol may remain in the body unaltered for 48 hours, and traces may persist for a week in serious poisoning Twenty to 70 per cent may be excreted through the lungs and 3 per cent through the urine.

Chronic poisoning is made possible by the cumulative effect from slow elimination.

Formaldehyde may be produced from methanol oxidation If so, it too is more toxic than is methanol, and persons poisoned with it may become profoundly acidotic.

Methyl alcohol produces poisoning by direct destruction and irritation of tissues and by a disturbed acid-base balance Methyl alcohol has unlimited miscibility with water but a very low solvent power for fats

Among all body fluids, the aqueous and vitreous of the eye have the highest percentage of water Thus it happens that intra-ocular fluid and unmedullated nervous tissues are sites of greatest damage from methanol

The direct local action of methanol and formic acid damages the gastrointestinal tract (especially the stomach), the lungs, the kidneys, the liver, the pancreas, the brain and, most markedly, the eyes The general action results in acidosis This is thought to be due largely to the formation of formic acid, and perhaps secondarily to the accumulation of carbon dioxide The latter is a consequence of the alveolar damage of methanol

Symptoms In general, patients who are mildly poisoned have symptoms indistinguishable from those of patients suffering the aftermaths of ordinary ethyl alcoholism. The symptoms consist of headache, dizziness, nausea, lassitude and slight abdominal pain Some patients on admission have violent epigastric pain, vomiting, delirium and various degrees of blindness.

Sometimes the symptoms of inebriation partially clear, just prior to coma, giving a false impression of recovery Coma frequently is accompanied with Kussmaul breathing, cyanosis, noisy gurgling respirations and, usually, respiratory arrest, circulatory collapse and death.

moderately, but is overcome by the irresistible impulse to drink excessively, even when he knows that drinking is injurious to his body and mind.

In chronic alcoholism there is often a chronic catarrh of the throat, larynx and stomach. There are an injection of the cutaneous vessels of the face and acne, or pustular eruptions Fatty degeneration occurs in the liver and in the arterial walls throughout the body. The heart may undergo fatty changes accompanied by dilatation and weakness Cirrhosis of the liver, which is common in alcoholics, develops in part because of thiamine deficiency. But repeated excessive doses of alcohol may also cause acute hepatic damage

Drunkards often appear to be healthy, of good color, well nourished and strong. Depending on their inherent physical stamina, sooner or later alcoholic cachexia will overtake them In alcoholic cachexia there are emaciation, pallor, cyanosis, tremulousness and unsteadiness, and an indifference and incapability.

Dipsomania In dipsomania, periodically there is an irresistible impulse to excessive drinking of alcoholic liquors After the first drink the patient begins to drink rapidly, of whiskey, brandy, or gin, without choice or purpose A single attack lasts, in most cases, about 3 days, but it may extend to a week or to two Subsequent to an attack, the patient is depressed and self-accusatory; he resolves never to take another drink, and he may be industrious and abstinent until the occurrence of the next attack The succeeding attacks occur more regularly and more frequently as time passes.

Dipsomania is manifested as a form of chronic alcoholism, but in reality it is a sign of a periodically recurring abnormal mental state.

Delirium Tremens This is a delirium of chronic drunkards, usually after many years of excess, it usually appears after a temporary abstinence from alcohol, due to gastric catarrh, to infection or to lack of access to alcoholic beverages.

The delirium comes on suddenly, lasts from 2 to 10 days, and is characterized by a dreamy alteration of consciousness, with visual hallucinations and illusions. The patients are especially prone to have visual hallucinations of a large number of small, moving, dark objects such as flies, mice, lice and snakes, and are greatly terrified by them

During an attack of violence there may be fever, tachycardia, tremor, anorexia and sweating. At the end of the attack the patient, if he is to recover, falls into a deep sleep and awakes with a clear consciousness, again fully oriented Death may occur from heart failure, from a complicating pneumonia, or from gastrointestinal manifestations.

If the patient's habits are known, there is usually little difficulty in arriving at the diagnosis If not, delirium tremens may be confused with other twilight states, hysteria and epilepsy, traumatic psychoses and infectious or toxic deliria.

Korsakoff's Psychosis (Polyneuritic Psychosis) This is a psychosis accompanied with polyneuritis which is commonest in alcoholism, though it occurs in other conditions that give rise to multiple neuritis The same psychosis may occur without the neuritis

There is an impairment of the recording faculty of the cerebral hemispheres which is manifested by forgetting immediately all new impressions and the most [illegible] emory falsifi- [illegible] iese falsifica- [illegible] liar has no [illegible] memory disturbances.

Cure is rare, chronic mental disease usually ensues.

Paranoid States Related to Alcoholism. In chronic alcoholism paranoid states are frequent These states are stages of alcoholism, for instance, the acute alcoholic paranoid state incident to acute alcoholism, and the jealous insanity of drunkards. The acute alcoholic paranoid state was discussed with acute alcoholic intoxication,

along with increased confidence in the powers, mental and physical. Larger quantities are followed by laughter, loquacity and gesticulation. The face becomes flushed and hot, the pupils become dilated, the eyes brighter and livelier; the pulse is accelerated Self-control is partially lost, the will power is weakened Movements are undignified, and there may be outbursts of anger, unreasonableness, and sensual fancies. The sense of responsibility, the power of judgment, and the regard for the feelings of others or the ordinary conventions of life are lost. The ingestion of more is followed by ataxic movements; the speech becomes difficult and stammering

The gait and locomotion resembles that observed in cerebellar ataxia. A deep sleep follows. On awakening from slumber, there are mental depression with nausea, vomiting and anorexia, which may last for several days, associated with the symptoms of acute gastrointestinal irritation and physical weakness.

The ingestion of 50 ml of alcohol induces irritation of the gastrointestinal tract with a profuse secretion of mucus The nausea and vomiting encountered may arise in part from this local irritation, but it is probable that the nervous centers are also involved directly as in the case of the general anesthetic agents which induce similar symptoms

Alcohol in moderate doses has a depressant effect on the motor and mental faculties Work requiring skill is done with decreased endurance, more slowly and with more errors than without it In some persons alcohol removes nervousness, self-consciousness and anxiety by depression of the higher inhibitory centers and in these it may contribute to better performance.

The stimulation observed following the ingestion of alcohol is a result of the removal of the inhibitory action of the cerebral cortex and the weakening of the will and self-restraint. The drug appears to act most strongly on the most recently acquired faculties, the power of self-control and the sense of responsibility. Alcohol is a narcotic which depresses first the highest cerebral center, and then the lower ones including the cerebellum and spinal cord

The manifestations of alcohol are characterized by a flushed, hot, perspiring face. The pulse is accelerated during the excitement of alcoholic intoxication Even small amounts of alcohol may cause a transient acceleration of the pulse and cardiac output and a slight rise in arterial pressure In moderate drinkers, slightly larger amounts cause appreciable increases in both blood pressure and cardiac output Alcohol is believed by some to augment the strength of the heart, but the change is small in extent and inconstant in its appearance. Larger quantities weaken the auricular and later the ventricular systole and induce dilatation and slowing of both chambers

Large quantities of alcohol lead to a deep sleep which eventually passes into total unconsciousness The respiration is stertorous and slow, and the face becomes pale or cyanotic. The pupils are dilated This condition may last for several hours and end in death from failure of the respiration When the stage of anesthesia is reached, it lasts much longer than that produced by chloroform or ether If unconsciousness lasts longer than 10 to 12 hours, recovery is unlikely. Death occurs, likely from edema and paralysis of the medullary centers

In the blood and urine of normal persons there is less than 0 1 per cent of alcohol Concentrations of 0.1 to 0.2 per cent in the blood and 0 25 per cent in the urine are accompanied by emotional instability and slight motor in-co-ordination. When the concentration reaches 0.2 to 0.35 per cent in the blood and 0 25 to 0 45 per cent in the urine there is confusion and ataxia of speech and gait Stupor is established with concentrations of 0.3 to 0 4 in the blood and concentrations of 0 5 to 0 7 in the urine It is in this range of alcoholic concentration in the blood and urine that death ensues Analyses of the blood and urine from the dead one are of no value unless made within an hour or two after death

Chronic Alcoholism. Men and women who become chronic alcoholics are predisposed by the inheritance of a bad nervous system. A drunkard cannot drink

the olefins, unsaturated, for example ethylene, propylene; and the naphthalenes. They are strong solvents, used as cleaners of metal and textiles, as solvents for rubber, tar and gums; as thinners of cellulose lacquers; for treatment of garbage, tankage and bones; in the production of high grade lubricating oils from inferior ones; and in the production of vegetable oils. They are used in fire extinguishers and refrigerators.

Monochlormethane (methyl chloride) (CH_3Cl) is used in refrigeration. It is a weak narcotic and a severe nerve poison. Refrigerator repairmen after chronic exposure may have attacks of dizziness and drunkenness, apathy, anorexia, persistent somnolence, loss of power in the legs, uncertain gait and disturbances of vision There may be anemia, jaundice and impaired or disturbed function of the kidneys.

Trichlormethane (chloroform) is no longer used extensively as a general anesthetic agent and therefore it is not an important cause of disability

Tetrachlormethane, known as carbon tetrachloride, is a noninflammable fluid used in chemical fire extinguishers and as a dry cleaner It is a narcotic with an action very like that of chloroform The after-effects of severe narcosis are more serious than are those of delayed chloroform poisoning

In man, poisoning by carbon tetrachloride produces symptoms of hepatic and renal injury Persistent headache, nausea, vomiting, diarrhea, pain, and tenderness in the hepatic region and jaundiced scleras characterize the early stages The renal injury is manifested by oliguria, the urine is heavy with albumin and casts. These manifestations follow those from hepatic injury Soon uremia, increasing in severity as the suppression of urine becomes complete, ends in death.

The recovery of renal function following acute renal failure due to carbon tetrachloride poisoning is characterized by three clinical phases The first phase starts with the cessation of oliguria and is associated with rising concentrations of creatinine and urea in the blood despite an adequate excretion of urine It lasts 1 to 3 days The second phase begins with a rapid decline in the concentrations of urea and creatinine After 5 to 6 weeks the renal functional activity begins to improve and slowly regains normal limits.

Chronic poisoning by carbon tetrachloride seems to be well established as an entity The symptoms are headache, vertigo, loss of appetite, gastric distress, loss of strength and, in some, jaundice

Monochlorethane (ethyl chloride) (C_2H_5Cl) is used as a local anesthetic agent, as a refrigerant, and as a solvent in making perfumes It is less toxic than methyl chloride (monochlormethane) but similar in its action

Dichlorethane (ethylene dichloride) is an excellent solvent and a dangerous poison It is used in dry cleaning, in the production of photographic films and as a thinner of lacquers, especially for coating the interior of beer vats. It is a narcotic poison and causes a severe dermatitis of the hands, leukocytosis and hepatic disturbance, but no evidence of renal involvement Fatal injuries are rare

Trichlorethane ($C_2H_3Cl_3$) when made from grape pips which are crushed and dried and distilled may endanger those near by its rapidly acting anesthetic fumes and by causing acute congestion of the lungs and kidneys and to a less extent of the liver and spleen Lesions of the skin are formed which resemble burns

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The jealous insanity of drunkards coincides with the deterioration of ethical standards and loss of self-respect and family respect. As the drunkard g older, he recalls his own amorous affairs away from home in his younger and di ing days. He realizes that he is still absent from home "just for drinking," for c he has become sexually impotent. If he should have a wife at home younger tha is, he suspects that she is having amorous relations with others The idea s becomes transformed into a fixed delusion and is supported by auditory and vi hallucinations The wife is often violently mistreated, and may even be murde The symptoms disappear after a few weeks of total abstinence in an asylum, c

solvent mixtures It causes keratitis, consisting in numerous translucent vacuole the superficial layers of an otherwise normal cornea These lesions may occur w out symptoms When symptoms are present, they consist of pain and epiphora m severe in the early morning *Amyl alcohol* ($C_5H_{11}OH$), commonly known as fu oil, is a poison when taken through the mouth, causing headache, dizziness, naus vomiting, diarrhea, delirium, coma and death

Furfural ($C_4H_3O.CHO$) is one of the essential constituents of Japanese r wine (saké) When fed to animals with rice in amounts varying from 10 to 50 per kilogram of body weight, furfural may produce early death Generally speaki rats fed on these amounts of furfural begin to show evidence of hepatic cirrho in 60 to 90 days; much smaller feedings of furfural may not lead to such a path logic condition until 300 to 500 days later

Oxalic Acid. The adverse effects of administration of oxalic acid are attribut to the formation of a highly insoluble precipitate with calcium. However, many the common articles of the diet contain oxalates and these substances continue be present in the blood and urine. The presence of oxalic acid in the blood and uri may be the result of its being a product of intermediary metabolism, particularly carbohydrate

The oxalate ion reduces the solubility of powdered dental enamel in solutic with an acid reaction There is some evidence that oxalic acid exerts a protecti action against erosion of the teeth by other acids

Poisoning from oxalic acid usually results from swallowing of a solution of in which case there is a marked corrosive effect involving mouth, esophagus, an stomach, with vomiting, intense burning pain, collapse, sometimes convulsions, an death The action of oxalic acid is the result of a chemical affinity for calcium, whic is drawn from the blood, with reduction of alkalinity of the blood and increase i the sugar content The renal tubules become obstructed by the insoluble calciur oxalate, and great disturbances in renal functional activity ensue.

Hexamethylenetetramine. Hexamethylenetetramine (urotropin) causes irri tation of the skin and, in excessive doses, of the urinary tract. In the urinary trac on decomposition it liberates formalin.

Nitroglycerin. Nitroglycerin is a main constituent of dynamite as well as a medicinal preparation. It is a vasodepressant and a common cause of "powde headache," or "dynamite headache." The face is flushed, and there are intense throbbing in the head, palpitation, and sometimes nausea, vomiting and polyuria

Formaldehyde. Formaldehyde (CH_2O) is a powerful irritant to the tissues with which it comes in contact, skin, conjunctivae and mucous membranes. This effect is due to the formation of an irreversible combination of formaldehyde with the protein of the surface cells.

Chlorinated Hydrocarbons. The chlorinated hydrocarbons are of the pe- ... series and are divided into the saturated (paraffin) group, methane, ethane,

the olefins, unsaturated, for example ethylene, propylene; and the naphthalenes. They are strong solvents, used as cleaners of metal and textiles; as solvents for rubber, tar and gums; as thinners of cellulose lacquers; for treatment of garbage, tankage and bones; in the production of high grade lubricating oils from inferior ones; and in the production of vegetable oils They are used in fire extinguishers and refrigerators.

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stinate than in delayed chloroform poisoning. The blood changes in moderate poisoning consist in a mononucleosis with increase of the lymphocytes.

Chloral (CCl_3CHO) is a soporific, intensely irritating vapor. Its action on the lungs is similar to that of phosgene and therefore it can produce fatal pulmonary edema.

Trichloroethylene $CHCl:CCl_2$ (C_2HCl_3) is noninflammable and has a strong narcotic action In acute poisoning there are excitement, drunkenness, or dullness and confusion. Death may ensue from the narcotic effect without the victim regaining consciousness. There is congestion and acute edema of the lungs, liver and kidneys It does not seem that sequelae result from acute poisoning, nor is there a chronic form of poisoning

Tetrachloroethylene ($CCl_2{\cdot}CCl_2$) is a safe substitute for carbon tetrachloride for hookworm therapy It can be used for the same purposes as trichloroethylene, and is a relatively harmless solvent.

Ethylene chlorohydrin (C_2H_4ClOH) may cause death from edema of the lungs and degeneration of kidneys There may be symptoms suggestive of a narcotic poison and the vomiting of bile-stained fluid. The liver and spleen may be swollen, hard, and intensely congested There is evidence that this solvent is a cumulative poison and that men of poor physique and women are more susceptible than healthy men.

Bromine Derivatives of the Hydrocarbons. The bromine compounds, methyl bromide, ethyl bromide and ethylene dibromide, are much more toxic than the chlorine compounds They are used as refrigerants and, in combination with carbon tetrachloride, as fire extinguishers Ethylene dibromide is used in tetraethyl lead gasoline to act as a catalyst.

Methyl bromide (CH_3Br) on the skin may cause painful burns with blistering. It has an apparent action on the basal ganglia and the cerebellum Methyl bromide has been used as a refrigerant, as a fire extinguisher and as a fumigant for cereals and seeds. It is shipped as a liquid in cylinders and either is allowed to evaporate directly into the fumigation area or is conveyed there by pipes

Methyl bromide is more toxic than either chloroform or carbon tetrachloride. When inhaled, it causes congestion of the lungs, edema, and injury to the vascular system as manifested by hemorrhage After a single exposure degenerative changes in the organs are observed, especially in the kidneys

Symptoms referable to the nervous system are manifest as headache, vertigo, paralyses, visual disturbances, delirium, psychic disturbances and even convulsions and coma Acute poisoning usually results in pulmonary irritation leading to bronchial pneumonia Anorexia, nausea and vomiting are seen most frequently, then headache, vertigo, difficulty in focusing the eyes, lethargy, gastrointestinal symptoms, muscular pains, faintness and dimness of vision. A vesicular burn, resembling a second degree burn, occurs when liquid methyl bromide comes in direct contact with the skin, and a late itching dermatitis will result from contact

In patients who recover from acute symptoms there has sometimes been evidence of lasting injury to the central nervous system After a transient narcosis there is a free interval of several hours or days, and then muscular twitchings and cramps begin, increasing to convulsions, coma and death

Ethyl bromide is nontoxic on inhalation

Carbon Disulfide. Carbon disulfide (CS_2) dissolves fats and gums, gutta-percha, and rubber. In the production of viscose rayon, cellulose is treated with an alkali to form alkali cellulose. This is changed to cellulose xanthate by being treated with carbon disulfide. The exposure to fumes of carbon disulfide takes place during this process

The commonest manifestation of carbon disulfide poisoning is a peripheral neuritis Usually the symptoms begin with parasthesias. Pain and tenderness are

soon associated with these symptoms and are distributed along the course of the nerve trunk. The senses of touch, pain, and temperature are heightened.

During the night, pain in the legs may reach an intolerable intensity. The radial, ulnar, sciatic, and external peroneal are the nerves commonly affected. Motor involvement is manifested by early fatigue and gradually increasing loss of strength Weakness in the legs appears earlier and is complained of more frequently than weakness in the arms. Sometimes there is an exaggeration of the deep tendon reflexes. As time passes, wasting appears according to the severity and duration of the poisoning The course of carbon disulfide neuritis is slow.

Turpentine. When turpentine was in general use by painters, they often complained of turpentine intoxication, which consists of periods of drowsiness, headache, nausea, loss of appetite, vomiting, vesical and renal complaints, inflammation of the eyes, irritation of the throat, bronchitis and cutaneous eruptions.

There is little real evidence of lasting injury to the kidneys, despite the belief of painters to the contrary During colonial days turpentine was often taken internally for renal complaints

Tobacco. Work with tobacco has been considered unhealthful but there are no objective data to bear out the accuracy of the belief.

Newcomers in tobacco handling experience the same symptoms as the inexperienced smoker—headache, palpitation of the heart, perhaps rapid, irregular pulse, nausea, and vomiting—but sooner or later an immunity is established It is often asserted that nicotine causes toxic amblyopia, just as do alcohol, lead and carbon disulfide, but examination of tobacco workers does not substantiate this assertion.

Synthetic Rubber. The toxic substances used in the production of rubbers are acrylonitrile or vinyl cyanide (see Cyanides, p. 1430) butadiene and monomeric styrene. Butadiene is mildly narcotic. The vapors cause irritation of eyes, nasal passages, throat, and lungs, sometimes with cough and also a sense of fatigue and drowsiness

Styrene causes irritation of eyes and nose, and the inhalation of styrene fumes causes light narcotic symptoms

Chlorobutadiene causes a loss of hair Men and women in contact with it experience loss of hair which is never patchy and is not long lasting, even if it goes on to total alopecia. Hair on the body is not affected, nor are eyebrows, and there is no accompanying dermatitis

There are numerous rubber solvents and many of them are toxic These solvents are often used in the manufacture and repair of shoes The solvents present in rubber cements are petroleum naphthas, benzol, toluol, xylol, cyclohexane and methycyclohexane, acetone, methyl ethyl ketone, carbon tetrachloride and trichloroethylene

Welding. The use of oxyacetylene torches in small, closed spaces creates a highly irritating dust or gas which may cause respiratory irritation and pneumonia Ferric oxide is contained in the gas, it acts like silicon in the lungs and cannot cause acute disease

Electric arc welding is attended with the production of ultraviolet rays, necessitating protection of eyes and skin, and a greater production of heat The intense odor of arc welding is from ozone. The possible dangers in welding may be summarized by enumeration of the toxic agents present, namely, ultraviolet rays, excessive heat, the volatile products of heated metals, zinc, lead, cadmium, fluorides, manganese, phosphorus, vanadium and chromium The composition of the welding rod is almost pure steel However, some rods are coated with a complicated mixture of organic and inorganic substances in addition to the forementioned metals. There is a greater production of nitrous gases, an accepted cause of lung fever, when bare rods are used, or of metallic fumes when the rods are coated.

Ocular injuries from welding are among the first effects to be noted. A welder

must protect not only himself and his eyes against the torch flame but also the men working near him.

Oil Folliculitis. Oil folliculitis or furunculosis is caused either by the plugging of sebaceous hair ducts or by the production of small abrasions by metal filings. All oils have a penetrative power, and almost all have an irritant action which causes swelling of the mouths of the sebaceous hair ducts, with production of blackheads and then retention cysts The entrance of pyogenic bacteria turns the cyst into an abscess, which discharges and heals, leaving a hole, so that after some time the skin is pock marked Oil boils can be prevented by using sawdust soaked in liquid soap and warm water, followed by gentle drying and covering the boils with lanolin or castor oil.

Riehl's melanosis or pigmented reticular poikiloderma is an occupational cutaneous affection which is connected with the use of mineral oil. There are dark patches of skin, often on the face, neck and folds of the axillae. The process begins with redness followed by patchy browning surrounded by a violet zone When the melanosis fades, the skin is left somewhat atrophic

Cruickshank and Squire called attention to cutaneous contamination of workmen where automatic machines are used which eject much oil The skin of the machine operators becomes grossly contaminated with cutting oils. Eight of every 10 workers observed by the writers were afflicted with oil folliculitis. In addition, workers who had been exposed for long periods had multiple hyperkeratotic lesions on their arms. Scrotal carcinoma was observed in one operator. An investigation of the records of the United Birmingham Hospitals revealed that during the last 10 years 34 instances of scrotal cancer occurred Of these, 6 occurred in machine operators and 6 in other workers exposed to oil in the engineering industry; 13 occurred in workers exposed to tar, pitch and similar products

Drug Addiction. In its broadest sense the term drug addiction applies to any person in whom for either physical or psychologic reasons a compelling need for certain drugs has developed.

Habit-forming drugs may be classified into two categories. the narcotic group, and the various types of sedatives and hypnotics

According to federal statutes, the narcotic drugs are opium and its derivatives, cocaine, marihuana, heroin and demerol, and addiction to these substances is legally narcotic drug addiction.

Himmelsbach stated that addiction to the opiate drugs embraces three related phenomena (1) tolerance or the gradual decrease in the effect produced by the repeated administration of a drug, (2) physical dependence, which is manifested by the appearance of a characteristic illness if the drug is withheld and (3) habituation or psychic dependence, which implies an intense desire for the repetition of pleasurable effects associated with the use of a drug.

In the nonnarcotic group are alcohol, paraldehyde, the various barbiturates, especially veronal, amphetamine or benzedrine, rarely ether by inhalation, and similar drugs These differ in the main from the narcotic group in that they do not produce a physical dependence and their rapid withdrawal is accompanied by very slight abstinence symptoms

There are two types of drug addicts: (1) the emotionally stable person who acquires the addiction accidentally, and whose normal personality make-up will be re-established after he recovers from his physical illness and is relieved from his drug addiction and (2) the psychopathic person who becomes an addict through curiosity or association, or as a sequence to his inadequate personality The prognosis as to relapses and the method of treatment are different in these two groups The first group can be rehabilitated.

Morphine and Morphine Addiction. As with alcohol, certain people have nervous systems unable to resist the tendency to relieve discomfort or depression

by morphine. It is especially common among those to whom morphine is easily accessible (druggists, physicians, veterinarians, registered nurses), though it sometimes develops in psychopathic patients following morphine therapy. Husband and wife not infrequently become simultaneous victims The hypodermic use is the commonest.

Once established, the habit is very hard to break. Many hypodermic injections are taken secretly each day. If the physician suspects it, verification can be made by finding the numerous, small, pigmented spots, corresponding to the sites of injection in the skin Cachexia gradually develops, with sallowness and emaciation, ethical defects, lying, egoism and loss of memory Sudden abstinence produces alarming symptoms such as restlessness, anxiety, despair, vomiting and delirium All of the manifestations are quickly relieved by a hypodermic injection of morphine

The patient's complaint is likely to be one which he has learned will often induce the physician to administer morphine. Seldom will the complaint be of the addiction itself.

Heroin (Diamorphine) and Heroin Addiction. Heroin is formed from morphine by substituting acetyl for hydroxyl groups. Its effects are very much the same as those of morphine but it affects the cerebrum and medulla more profoundly than morphine.

Heroin addiction is easily acquired due to the ease of administration of small quantities of the drugs by snuffing or by hypodermic injections. Addiction causes rapid changes in the personality, utter disregard for moral standards and conventions, and the addict rapidly becomes a mental and moral degenerate The habit is exceedingly difficult to cure, not only in the active withdrawal period but also in the convalescent stage, and relapse is frequent. The manufacture and importation of heroin has been outlawed in the United States.

Cocaine and Cocaine Addiction. In the cocaine habit the deterioration progresses more rapidly than in the morphine habit Very frequently morphinism and cocainism are associated In the cocaine habitude acute hallucinatory confusion often develops Withdrawal symptoms in the cocaine habit are milder and disappear more quickly than in the morphine habit

Here again the complaint is unlikely to be sincere if made by the patient himself

Demerol Hydrochloride and Demerol Addiction. Demerol, ethyl 1-methyl-4-phenylpiperidine-4-carboxylate hydrochloride, is a proprietary analgesic, spasmolytic and sedative drug which is administered orally or intramuscularly in doses of 50 to 150 mg Addiction to this drug is not uncommon.

Hazards from Agricultural Chemicals (Pesticides). In recent years atten-

poisonous Dangerous quantities of these substances may enter the body through the lungs, by absorption through the skin, or by swallowing.

Protection against the hazard of poisoning is effected by the use of personal protective measures, proper design and installation of spraying and dusting equipment and the employment of operational procedures which minimize exposure. The personal protective measures include avoiding contact with the skin by the use of shirts buttoned at the wrist, the wearing of gloves; the prompt washing with soap and water of any part of the skin that comes in contact with the chemical, and the replacement of contaminated clothing with clean clothing, avoidance of inhalation of dust, mist, spray or aerosol containing the chemical and the use of appropriate breathing equipment if there is any suspicion of the pilot's being harmfully affected; the avoidance of contamination of food, refusal to eat, smoke or drink in the dusting or spraying area and the washing of hands and face before eating or using tobacco; protection of the eyes with goggles,

since some of the insecticides, for example, the organic phosphates, can harmfully affect vision. A bath, followed by the use of freshly laundered clothing, should be taken after handling or coming near these chemicals

Organic Phosphorus Insecticides. The toxic manifestations of the organic phosphorus insecticides are similar and are referable to the postganglionic cholinergic nerves (muscarine-like effects), the preganglionic and somatic motor nerves (nicotine-like effects) and the central nervous system The muscarine-like effects are the earliest and commonest signs of poisoning

These chemicals do not produce local inflammatory changes in the skin. When symptoms begin, there may be little warning of impending serious effects

MUSCARINE-LIKE EFFECTS. The first symptoms to appear are usually anorexia and nausea These are soon followed by vomiting, abdominal cramps, excessive sweating, and salivation. If the exposure is extensive, diarrhea, tenesmus, involuntary defecation and urination, pallor, pinpoint nonreactive pupils, blurred vision, excessive bronchial secretion, sometimes respiratory difficulty and pulmonary edema with cyanosis ensue The respiratory manifestations are severest when the respiratory tract is one of the routes of absorption. Elevation of the blood pressure is common during severe intoxication due to parathion

NICOTINE-LIKE EFFECTS Muscular fasciculations in the eyelids and tongue are early signs If the exposure is extensive, these are followed by fasciculations in the muscles of the face and neck and in the extra-ocular muscles (resulting in jerking movements of the eyes) and then by generalized fasciculations and weakness In the severest cases there may be weakness of the muscles of respiration

EFFECTS ON THE CENTRAL NERVOUS SYSTEM. Giddiness, uneasiness, restlessness, anxiety and tremulousness occur early, followed by headache and sometimes by the sensation of "floating," insomnia and excessive dreaming. If the exposure is extensive, ataxia, tremor, drowsiness, difficulty in concentrating, mental confusion and occasionally disorientation develop Paresthesias are common after exposure to TEPP, while changes in speech consisting of slurring, difficulty in forming words and multiple repetition of the last syllable may occur after exposure to parathion. In very severe cases this stage is followed by coma, with the disappearance of all reflexes, and then by generalized convulsions During the coma there may be Cheyne-Stokes respiration

In poisoning due to the organic phosphorus insecticides 2 mg. of atropine is administered intramuscularly at hourly intervals, or more often if necessary, until signs of atropinization appear. The dose of atropine may then be reduced, but its administration should be continued as long as any muscarine-like symptoms are present Atropine should not be administered prophylactically

DDT (*Chlorophenothane U S P*) DDT is the abbreviated name for the various mixtures of para, para prime (p,p') and ortho, para prime (o,p') isomers of dichloro-diphenyl-trichloro-ethane which are used for insecticidal and *medicinal* purposes.

In therapeutics, DDT is used as a pediculicide and in conjunction with benzyl benzoate and ethylaminobenzoate as a pediculicide and scabicide A mixture of these compounds has been accepted for inclusion in *New and Nonofficial Remedies* for the treatment of scabies and pediculosis. DDT is official in the *United States Pharmacopoeia*, 14th Revision, under the name Chlorophenothane.

Acute poisoning from the absorption of crystalline DDT either through the skin or through the respiratory tract is unlikely, and large oral doses of the undissolved chemical must be ingested to produce symptoms of acute intoxication DDT in lipoid solvents has a greater tendency than in other mediums to be absorbed from the skin and the gastrointestinal tract and is therefore dangerous The intrinsic toxicity of DDT is about the same for insects and mammals.

kilogram of body weight or about 1 ounce of the solid material for the average person. Ingestion of massive amounts of powdered formulations of the chemical produces acute poisoning in spite of the fact that much of the material may be removed by vomiting.

Chronic DDT poisoning may result from the ingestion of small amounts of the material over a long time. Since the chemical is irregularly absorbed, the level below which adverse long range effects are absent is unknown

Powdered DDT rarely is toxic or irritating to the *intact skin*. An oily layer of sebum on the skin or the presence of greasy solvents on the integument increases absorption of DDT. Certain solvents and other additives incorporated into DDT formulations are capable of producing irritation of the skin and mucous membranes

DDT is not considered harmful to the *eyes*, since ointments and solutions up to 5 per cent have been used without ill effects. Powdered DDT thrown into the eye is not more irritating than other fine crystalline material.

The *inhalation* of DDT powder offers little hazard because of the large particle size and the relative insolubility of the compound Certain supposedly inert diluents used in the formulation of DDT wettable powders may irritate the bronchi, producing a persistent cough

The symptoms of DDT poisoning commence with twitching of the eyelids which progresses until severe generalized tremors become apparent. The tremors are coarse; they begin in the muscles of the head and neck, then progress caudally to involve the entire musculature with increasing intensity They are particularly severe in the extremities The convulsive seizures are similar to those encountered in strychnine poisoning and are elicited by irritation and mechanical stimuli such as sudden noises and jarring Death usually results from respiratory failure, although heart failure induced by ventricular fibrillation may intervene Pulmonary edema is common to solvent poisoning and is not characteristic of DDT.

Chronic intoxication may be manifested by loss of weight, anorexia, mild anemia, muscular weakness and tremors that terminate in convulsive seizures, coma and death

Diagnosis of DDT poisoning is based on the history of exposure and the presence of the foregoing-enumerated characteristic neurologic manifestations Tests of hepatic function may reveal injury to the liver due to prolonged exposure to DDT.

Solvents used in the formulation of DDT preparations, particularly kerosene, often produce symptoms which simulate those of acute DDT poisoning The signs of solvent intoxication set in promptly, in contrast to the latent period of several hours required for the development of DDT symptoms.

TREATMENT The treatment of acute DDT poisoning is directed toward removing DDT from the alimentary tract and allaying neurologic manifestations.

Benzene Hexachloride and Its Principal Isomers. Benzene hexachloride is an insecticidal agent. Although incorrect chemically, the name benzene hexachloride and its abbreviation, BHC, have been generally accepted as common designations for commercial mixtures of the stereoisomers of 1, 2, 3, 4, 5, 6-hexachlorocyclohexane The gamma isomer is of greatest entomologic and medical interest Lindane is the coined, common name for essentially pure grades of this isomer which are used for agricultural and related purposes The generic name, gamma benzene hexachloride, has been adopted

The gamma isomer is a strong excitant of the central nervous system The delta isomer is a depressant of the
ing effects of the gamma isom
in their action The alpha is
which is followed by depression, and the beta constituent provokes tremors and then depression of the central nervous system on prolonged administration.

The presence of fat or other lipoids facilitates penetration of the intestinal barrier. *Cutaneous absorption* of the material from oil solutions has been firmly established. Absorption of dusts from the skin is known to occur

Benzene hexachloride gives pathologic changes resembling those of DDT, with

hepatic damage the most prominent feature There is a moderate degree of hyaline granular degeneration of the renal convoluted tubular epithelium, and there are as well mild changes in the bone marrow, lymphoid tissues, adrenal cortex, and cerebrum Considered anatomically, these lesions have not always been sufficient to cause death However, all isomers may cause a general emaciation, and atrophy of various tissues

The symptoms of acute poisoning from technical benzene hexachloride are excitation, clonic-tonic convulsions, followed by hyperirritability to external stimuli and, finally, depression. Intoxication from benzene hexachloride of high gamma content or from the gamma isomer alone is manifested by restlessness, micturition, intermittent muscular spasm, loss of equilibrium, convulsions, and then collapse and death

The course of symptoms depends largely on the direct proportion to the amount of gamma isomer which is present. The immediate cause of death is functional disturbances of the central nervous system, and especially of the respiratory center.

Chronic symptoms are predominantly those of nervousness and lack of co-ordination, their severity depending on the frequency and the degree of exposure. Nausea, loss of weight, and general emaciation are manifestations of this type of exposure to the technical mixture.

The diagnosis of benzene hexachloride poisoning should be based mainly on a history of exposure to the product since poisoning by other pesticides, as well as the presence of other neurologic conditions, should be considered.

There is no specific antidote for poisoning from benzene hexachloride or its gamma isomer

Hair Dressings. The technics employed at the beauty parlor which may be of particular medical interest are (1) hair dyeing and (2) hair waving, the permanent wave

Hair Dyeing. Hair dyes have been in use as long as dyes have been employed for any purposes These dyes may be solely of vegetable or of mineral origin or they may be synthetic Some dyes are compounded from one or more of the basic materials.

The *vegetable dyes* are generally less likely to cause dermatitis or systemic effects from their use than are the mineral or the synthetic dyes. The extract from the green hulls of the American walnut turns the hair yellow or brown. The powdered leaves of *Lawsonia inermis*, a tropical shrub, are widely used to dye the hair a henna or a red color In recent years a vegetable dye is used by aging ladies to turn gray hair a blue color. The vegetable dyes are generally devoid of cutaneous or systemic effects.

The *metallic dyes* have been widely used Silver hair dyes too are generally harmless They can be employed to form blond, brown and black hair colors Nickel, cobalt, iron and silver can be used alone or in combination with pyrogallol to form almost any desired color for the hair

Of the numerous *synthetic hair dyes* the following are the compounds employed which may give local or systemic effects amino-anisole, p-aminodimethylaniline, p-aminodimethylamine, chloroaminophenols, chlorodiamines, diaminophenols, nitrodiamino compounds and toluylene diamine

The *compound hair dyes* are numerous and in recent years they are the dyes most commonly used For example, henna is often compounded with diamines or pyrogallol.

Hair dyes are potential skin irritants The compound and synthetic dyes are more likely to cause local or systemic effects. However, only a small proportion of those exposed acquire sensitization A patch test should be carried out before each application of a para dye, whether the dye is used for the whole head or for touching up. All reputable hairdressers recognize that this test should be done, but the client may be impatient. Some clients and beauticians believe that, once the hair has been dyed without ill effect, any dye can be used thenceforward without fear. Allergic sensitization, however, may develop after prolonged periods of use of the same dye or it may be present on the first application of another dye

No hair dyes should be applied during pregnancy or menstruation or in the presence of eczema or dermatitis on any part of the body. It is also best to avoid

them if the general health is poor They should never be used in the presence of hay fever or of asthma. They must never be applied to eyebrows or eyelashes.

The Permanent Wave. The technic of cold waving can produce local irritation of the skin Some persons appear to be more susceptible to this irritation than others. Some factors which may be considered are the differences in the materials employed and the technics of their use. Rarely, eczematous hypersensitivity may be produced in the cold waving process It seems that this eczematous hypersensitivity is more frequently due to materials other than the cold waving solutions themselves and, as Schwartz and Peck mentioned, especially the perfumes, gums and resins Ammonium thioglycolate is potentially a mild irritant for the skin.

When ammonium thioglycolate is used, despite considerable caution dermatitis may occur about the neck from the seepage between towels and the surface of the neck. Similarly, the dermatitis of the scalp may be due to unduly prolonged contact of the ammonium thioglycolate with the scalp, to inadequate removal of the material after its effect has been achieved, or to its incomplete neutralization at the proper time. Ammonium thioglycolate causes more cutaneous injury to beauty parlor operators than to the patrons.

The specific cause of a skin irritation sustained at a beauty parlor can rarely be proved by the diagnostic procedures available at present, since the lesions are nonspecific, being those of primary irritation

INORGANIC COMPOUNDS

Alkalies. The common caustic alkalies which produce injury and are often the concern of the physician are the hydrates of sodium, potassium and ammonium The anhydrous sodium carbonate (soda ash), calcium oxide (quicklime), calcium chloride, barium oxide and hydrate, the sulfides of sodium, calcium, arsenic, and the alums too have caustic properties. Quicklime, the alums and the sulfides will rarely be responsible for anything worse than dermatitis and conjunctivitis Caustic soda or potash may cause fatal burns or blindness, and severe injury may follow the splashing of ammonia into the eye, resulting in inflammation of conjunctiva and cornea, followed by atrophy of the iris and opacity of the lens The fumes of ammonia may cause death from congestion and edema of the lungs. Ammonia gas is very irritating to the upper air passages. If the escape is delayed, the gas may be deeply inhaled and may cause congestion of the lungs followed by edema, bronchial irritation and hemoptysis and, in some instances, death from pulmonary edema.

Inorganic Acids. The inorganic acids are known as mineral or heavy acids. The common ones which are prone to produce injury are sulfuric, hydrochloric, nitric, and hydrofluoric acids Their physiologic actions are the same as those of sulfur dioxide, chlorine, phosgene and the nitrogen oxides, but since the latter are gases, they are far more dangerous than are the acids, which usually cause no severer damage than caustic burns of skin or eyes. Nitric and hydrofluoric acids have a solvent action on metals and clay, and give rise to leaks in containers The burns from handling such weakened containers are more serious than those received otherwise from these acids Hydrofluoric acid is intensely caustic.

Acute poisoning from *hydrochloric acid* occurs usually from leaking chlorine cylinders or from the apparatus used to disinfect water. Chlorine injury produces tracheobronchitis and pulmonary edema Pneumonia may develop as a sequence of the respiratory irritation

Phosgene ($COCl_2$) is a deadly gas used as an intermediate in the production of aniline dyes, and it may also be encountered as a decomposition product of chlorinated hydrocarbons.

Phosgene hydrolyzes in the presence of water, forming hydrochloric acid gas

within the bronchial tubes There is consequently no protective respiratory reflex to prevent the deep inspiration of this gas In the alveoli the newly formed hydrochloric acid gas is liberated, causing congestion and edema which may be quickly fatal. If death does not occur, lobular pneumonia ensues. In the acute stage of the injury, which is in reality asphyxia, there is a high erythrocyte count, and increased hemoglobin

Nitric acid is dangerous because its fumes are composed of a series of anhydrides and various oxides which are liberated on exposure of nitric acid to the air. These fumes do not stimulate violent respiratory reflex. Thus the poisoning may be of an insidious onset.

Poisoning may occur in association with the manufacture of explosives. Explosives are nitrated products formed by the action of nitric acid on cellulose, glycerin, phenol, benzol and toluol. Nitrocellulose is the basis for smokeless powder, lacquers, and photographic films and celluloid. Nitrobenzol and nitrophenols are used in the production of drugs, dyes, and explosives

Nitric acid is used in metal etching and photoengraving and for cleaning ("bright dipping") copper and brass

Nitrogen peroxide, a main component of nitric acid fumes, or having other sources of origin, may cause almost immediate death However, the usual onset of symptoms is from 6 to 48 hours after exposure. First there is dyspnea, which increases rapidly as the acute pulmonary congestion is supplanted by edema If all the bronchial tree has been affected, death follows within 36 hours There are those, however, who recover from the immediate effects of the gas and have pneumonia later on. In addition to the action on the lungs, there may be intense congestion of the meninges and the cerebrum. A continued exposure to diluted nitrous fumes causes headache, sleeplessness, anorexia and gradual loss of strength, dyspepsia, constipation, sometimes ulcers on the lips and on the mucous membrane of the mouth and pharynx These manifestations clear up when exposure to the fumes ceases.

The venous blood is thick, coagulates rapidly, and turns red when diluted with water The nitrites which are formed in the blood produce their characteristic vasodepressant effect in a subject who has a severe or a rapidly fatal poisoning Destruction of erythrocytes, lesions in liver and kidneys, and an increasing jaundice may be present.

Dynamite contains nitroglycerin, and farmers and laborers who are not meticulous in protecting themselves from the postexplosive fumes of dynamite may have a cough, headache, and sensations of fullness in head and chest. These effects pass away on rest.

Hydrogen fluoride and its compounds are caustic, corrosive to the skin, the conjunctivae, and the mucous membranes The acid is used in etching and clouding of glass, cleaning sandstone and marble, in pickling metal, removing enamel from defective porcelain, treating textiles to remove the weighting metals, and it as well as its salts may be added to laundry mixtures. Hydrofluoric acid may be employed as a catalyst in the production of high-octane aviation fluid.

Fluorine compounds (cryolite and barium fluosilicate) are often contained in insecticidal sprays for fruits and vegetables and in phosphate rock which is mined and converted to superphosphate, which is used as fertilizer. The fluorides may be used in bleaching of cane for furniture, in the disinfection of hides (silicofluorides), and in poison for rats and cockroaches

Fluoride in domestic water supplies is a causative factor in dental fluorosis, or mottled enamel. Intensive investigation has been made of the physiologic chemistry of this element with respect to its influence on the skeleton, its metabolic effects and its relation to dental caries In view of the observation that fluorine in the drinking water is correlated with a significant decrease in dental caries, suggestions

have been made that fluoride be added to city water supplies in areas where this element is absent. However, the need for caution has been expressed for fear of the occurrence of less desirable effects of ingested fluoride such as a decrease in breaking strength of bones when fluoride in abundance is present in the diet or in the water.

Older persons subjected to excessive amounts of fluorine may develop an osteopathy of the osteitis fibrosa type. There are successively destruction of bone, osteoclasis, a progressive atrophy, then an osseous regeneration, and osteosclerosis. Roholm recorded that men who work with cryolite excrete large quantities of fluorine in the urine, a condition which persists for years afterward, since the fluorine is constantly mobilized from the bones.

Sodium fluoride may be eaten with food and not discovered by taste. Vomiting and diarrhea caused by ingestion of the chemical are often effective in eliminating much of the poison and thus make it difficult to determine the fatal dosage for man.

Nausea, vomiting, and diarrhea occur immediately and at times simultaneously in sodium fluoride poisoning. In many instances blood is present in the vomitus and stools. Soon after eating, the patients may complain of abdominal burning and cramps In some cases local or generalized urticaria may occur In all there is a thick, mucoid discharge from the nose and mouth General collapse may occur at varying periods of time but some hours after ingestion. Death may follow in from 2 to 4 hours In severe poisoning, when death is delayed for 18 to 20 hours, paralysis of the muscles of deglutition, carpopedal spasm, and spasm of the extremities occur Convulsions, abdominal tenderness, and rigidity are absent

The metal *chromium* is inert. *Chromic acid* and the chromates produce very painful and very obstinate lesions of mucous membranes, skin, and conjunctivae

The term holes applies to the ulcers caused by chromates because these ulcers slowly penetrate, burrow deep under the skin, and rarely suppurate. If the lesions or holes are serious enough to cause disability, it is prolonged, for these chronic ulcers heal slowly. The holes are usually situated around the fingernails, on the knuckles, the forearms, rarely on the toes. Sometimes the eyelids and the nasal mucosa may be affected by ulcers, which may cause disability owing to the severity of the pain

Ulcers of the nose are characteristically painless and chronic, are confined to the cartilaginous portion of the septum, and do not involve the bone or cause deformity. Progression of the lesion results in a perforation of the septum Perforation usually causes but little discomfort. In some, however, there is discomfort such as mouth breathing because of the constant formation of crusts. Rarely, the patient is aware of a whistling sound on nose breathing after the perforation has become established

Hydrobromic Acid. Hydrobromic acid (HBr) is a mineral acid, chemically a halogen acid, closely related to hydrochloric acid Injuries from it are the same as those from mineral acids in general.

Hydrobromic acid and its salts such as sodium, potassium and strontium bromide are used therapeutically as sedatives

Bromic acid ($HBrO_3$) has powerful oxidizing action The sodium salt is used in mixture with bromide for dissolving gold from its ores, and the potassium salt is used as an oxidizing agent in certain preparations for giving cold wave hair permanents The ingestion of salts of bromic acid causes immediate vomiting, and is followed by injury to the liver and the kidneys

Bromide Intoxication. Some proprietary medicines such as bromoseltzer, neurosine, sedormid and B C. headache powder contain bromides.

Bromides, like chlorides, are equally distributed in the extracellular spaces and soon reach a concentration in these regions corresponding to that in the blood stream. They are found in smaller amounts in the brain and in the spinal cord. This

may be one of the reasons, in addition to other factors, why it apparently requires varying quantities of bromides to produce central nervous system symptoms in different persons. Concentrations of plasma bromides in bromide intoxication vary widely. They may reach 150 mg per 100 ml. before there is intoxication.

With such variations in blood bromide levels, it is concluded that a number of factors other than the absolute dose of bromide are concerned in the development of bromide intoxication. A reduction of chloride in the diet is found to be effective in increasing the blood bromide concentration on a constant bromide intake. Wuth expressed the belief that intoxication begins at 25 per cent replacement of the blood chlorides and that 40 per cent replacement is fatal Renal injury, by interfering with bromide excretion, may produce the same effect.

Bromidism may be present in patients who either resort to self-medication or are given the drug by physicians. In either case there is a tendency by certain psychoneurotic patients to use the agent in increasing amounts over long periods of time.

In bromide intoxication there may be slowed mental processes and speech, ataxia and tremors of the hands Hallucinatory tendencies may occur, but definite hallucinosis is rare. Paranoid delusions are frequent. In acute intoxication delirium may be present.

The diagnosis is made on the history, symptoms, and the presence of increased (100 mg or more) concentrations of blood bromides. It is well to know, however, that the concentration of bromides may reach 150 mg per 100 ml. of blood without producing symptoms

A recent method of treatment of bromide intoxication is the judicious intravenous administration of physiologic salt solution

Boric Acid. Boric acid, whether applied in the form of an ointment or a saturated solution to extensive wounds, is to be considered a cumulative poison It may be absorbed in toxic quantities from ointments applied to burned areas or to wounds involving loss or injury to large areas of skin Of a 5 per cent boric acid solution used to irrigate cavities, most of the boric acid is absorbed by the tissues

Boric acid is not toxic when administered in a single large dose; however, repeated doses result in accumulation in the brain, liver and body fat After absorption boron occurs in both the white matter and the gray matter of all parts of the central nervous system and in the peripheral nerves. The spinal cord and the gray matter of the cerebrum contain the highest amounts. The boron found in the brain is not combined with phospholipids or cholesterol

Death is due to a shocklike syndrome which ensues as the result of sufficient amounts of boron quickly absorbed to produce poisoning If moderate doses of boron are given over a period of several days, or if the substance is slowly absorbed from a wound, death may result from inanition Even in the slow poisoning death is preceded by convulsive tremors and meningismus

Lead. Lead is amphoteric and occurs in nature as *galena* or lead sulfide (PbS). The lead sulfide is heated until a part of the sulfide is converted to lead monoxide, or lead oxide (PbO) and lead sulfate ($PbSO_4$). Lead is often combined with other metals for particular purposes, for instance an alloy of lead containing arsenic (0 5 per cent) is used in making shot and shrapnel bullets: type-metal contains from 20 to 25 per cent antimony; and solder contains 50 per cent tin The principal uses of lead are in storage batteries, paints, and as tetraethyl lead in gasoline

There are five oxides of lead Of these oxides the lead monoxide, or lead oxide (PbO), a solid crystalline yellowish red mass, is called *litharge;* the powdery form is called *massicot*

The basic carbonate is white lead, often manufactured by the old Dutch process and used in house paints. The sugar of lead used in medicine is ($Pb[CO_2CH_3]_2{\cdot}3H_2O$), an acetate of lead.

Lead suboxide may be present in the dust wherever solid lead is handled, and in the

fumes from molten lead Exposure to lead suboxide occurs in smelting zinc, in type founding, in founding brass, bronze, bearing metal, and babbitt, for these materials are of high lead content Exposure to lead occurs in soldering, in making molded lead materials and finishing them, and sometimes in the printer's trade

The use of solder as in brass founding may be attended with the production of lead fumes, and thus lead poisoning. Metallic lead particles in the lung act much as do silica particles, originating a fibrotic process.

Litharge (red lead, orange mineral) is employed extensively in many industries and in common work, for example in the manufacture of rubber glaze for pottery and tiles, and lead glass and varnish, in making storage batteries, in glazes, enamels for cast iron and sheet iron, and in paint.

White lead is readily soluble in human gastric juice It is responsible for the lead poisoning of painters, of most pottery workers, and of lithotransfer-makers The dust produced in dry sandpapering of painted surfaces and in handling of dry glazed ware, is a common source of the poisoning. The making of lithotransfer paper is a dangerous occupation in this regard, because of scattering of finely ground lead colors on the lithotransfer paper The chromates of lead, yellow and green, give little trouble, for paints containing these salts are used chiefly as exterior paints. In soluble lead glaze of some non-American pottery, the white lead is added after the fusion of the borates, silicates, and like substances, and is therefore unchanged It thus remains as a poorly soluble silicate, and borosilicate Fritted glaze as manufactured in American potteries is no longer a source of lead poisoning

The degree of risk of lead poisoning in mining lead ores depends on the presence of soluble ores Lead sulfate and carbonate are for practical purposes insoluble.

Tetraethyl lead as it occurs in gasoline is rapidly absorbed and soluble in fats, which leads to its concentration in the central nervous system and in the liver. All who handle and use gasoline containing lead are constantly warned by appropriate signs on gasoline pumps of its injurious effects

The manifestations of plumbism differ according to the degree of exposure, the solubility of the lead, the individual size of the particles of the lead compounds, and the concentration of the fumes or dust in the air Exposure to heavy amounts of soluble lead compounds may occur when heavy doses of lead fumes are obtained, resulting in severe acute plumbism As in almost every other poison or infection there are persons who have an increased susceptibility and therefore may be severely poisoned by relatively small doses of lead In such a susceptible person wristdrop, ankledrop or an encephalopathy may develop after there has been exposure only long enough to make one lead soldering

Swallowed lead is excreted in feces Absorption through the skin, except in the case of tetraethyl lead, is not an important source of plumbism Absorption from the respiratory tract is rapid due to the fact that inspired lead enters directly into the general circulation instead of passing through the liver as in gastrointestinal absorption. In the gastrointestinal tract, absorption is depressed by the presence of soluble phosphates which prevent solubility of particulate lead or force soluble lead out of solution

PATHOLOGY. Changes in the vascular system resulting in multiple small hemorrhages and in thickening of the walls of the blood vessels are commoner than any other pathologic change

Volhard assumed that lead causes spasmodic contraction of the smooth muscle fibers of the *renal blood vessels*, and that this results in ischemia followed by parenchymatous degeneration, a saturnine nephritis which is closely associated with the attacks of colic.

Lead is temporarily stored in the liver before elimination. It damages the liver, as revealed by slight jaundice and by indirect reaction to the van den Bergh test.

The lesion in the peripheral nerves is an atrophic degenerative neuritis, with subsequent fibrosis It is distinguishable from paralysis following actual lesions of the cord The lesion in the nerve is periaxial which explains the reversibility of lead palsy There is a marked atrophy of the affected muscles

Muscles affected by lead palsy are not supplied by the same nerve nor are all the muscles affected which a single nerve supplies Aub is inclined to find the cause of lead palsy in the metabolism of the muscle

may be one of the reasons, in addition to other factors, why it apparently requires varying quantities of bromides to produce central nervous system symptoms in different persons. Concentrations of plasma bromides in bromide intoxication vary widely. They may reach 150 mg. per 100 ml. before there is intoxication.

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Boric Acid. Boric acid, whether applied in the form of an ointment or a saturated solution to extensive wounds, is to be considered a cumulative poison. It may be absorbed in toxic quantities from ointments applied to burned areas or to wounds involving loss or injury to large areas of skin Of a 5 per cent boric acid solution used to irrigate cavities, most of the boric acid is absorbed by the tissues

Boric acid is not toxic when administered in a single large dose, however, repeated doses result in accumulation in the brain, liver and body fat. After absorption boron occurs in both the white matter and the gray matter of all parts of the central nervous system and in the peripheral nerves The spinal cord and the gray matter of the cerebrum contain the highest amounts. The boron found in the brain is not combined with phospholipids or cholesterol.

Death is due to a shocklike syndrome which ensues as the result of sufficient amounts of boron quickly absorbed to produce poisoning If moderate doses of boron are given over a period of several days, or if the substance is slowly absorbed from a wound, death may result from inanition. Even in the slow poisoning death is preceded by convulsive tremors and meningismus

Lead. Lead is amphoteric and occurs in nature as *galena* or lead sulfide (PbS) The lead sulfide is heated until a part of the sulfide is converted to lead monoxide, or lead oxide (PbO) and lead sulfate ($PbSO_4$) Lead is often combined with other metals for particular purposes, for instance an alloy of lead containing arsenic (0 5 per cent) is used in making shot and shrapnel bullets; type-metal contains from 20 to 25 per cent antimony, and solder contains 50 per cent tin The principal uses of lead are in storage batteries, paints, and as tetraethyl lead in gasoline

There are five oxides of lead Of these oxides the lead monoxide, or lead oxide (PbO), a solid crystalline yellowish red mass, is called *litharge;* the powdery form is called *massicot.*

The basic carbonate is white lead, often manufactured by the old Dutch process and used in house paints The sugar of lead used in medicine is ($Pb[CO_2CH_3]_2, 3H_2O$), an acetate of lead.

Lead suboxide may be present in the dust wherever solid lead is handled, and in the

frequency to be useful diagnostic aids. Stipple cells are present in normal persons. In hepatic cirrhosis, pulmonary disease, and especially in hemolytic crises, stipple cell counts as high as 40,000 to 50,000 per million of erythrocytes may be present without associated exposure to lead. However, usually lead absorption is accompanied by an increased stipple cell count Basophilic stippling becomes significant in lead absorption when the range of stipple cells is known for a particular individual Increases then would indicate exposure to lead and would be evidence in favor of the diagnosis of lead intoxication The degree of reduction in hemoglobin is never great in lead intoxication

The New York Division of Industrial Hygiene has adopted the following standard for practical use in determining *lead absorption in excess of normal*

Urine Lead in urine in excess of 0.1 mg. of lead per liter of urine indicates an excretion of lead above that which one would ordinarily expect

Feces. Lead in the feces in excess of 0 5 mg. of lead per gm of ash may be regarded as higher than normal

Blood. Lead in whole blood in excess of 0 07 mg. per 100 ml of blood may be regarded as higher than normal

The irregularity with which porphyrinuria occurs in lead poisoning has discouraged reliance on its presence as a diagnostic aid in lead poisoning

The presence of lead in urine and blood in excess of the normal does not prove lead intoxication, only absorption. Lead in the feces does not prove even that, for the lead may have passed through the intestinal tract without being absorbed at all.

Diagnosis of Lead Poisoning The diagnosis of lead poisoning may not be difficult if there is a history of exposure to lead The intensity, the duration, whether the exposure was recent or some years previous to the examination, whether the lead compound was one of the readily soluble or one of the poorly soluble compounds are important data for diagnostic purposes However, the diagnosis of lead poisoning in practice depends on obtaining evidence of lead poisoning and then determining a possible source of lead sufficient to cause poisoning Gastrointestinal disturbances with or without colic, pains in the joints and muscles, tremors, rarely with palsy, headache and disturbed sleep are the usual symptoms of plumbism In addition to these symptoms there are the presence in the urine of concentrations of 0 04 mg of lead per liter and the presence of basophilic stippling of the erythrocytes in the absence of a severe anemia.

Mercury. The sources of mercurialism are mining of mercury, the treatment of fur with mercury nitrate and the treatment of seeds and grain It is rare, in recent times, for mercurialism to be caused by the administrations of mercury by mouth or intramuscularly

Cinnabar (HgS) is insoluble in the body fluids Miners often work alternately between mining and metallurgy In the metallurgy of mercury, metallic mercury is collected in condensers made of tile or wood Quicksilver penetrates these substances, working its way through the lining of the furnace, iron pipes, fire bricks, terra cotta and the sides of the condensers so that periodic cleansing of this equipment is necessary It is during this changing process that laborers may contract mercurialism

[illegible]

portable radios and miniature flashlights

The occurrence of chronic mercurialism among dentists is a result of continual handling of amalgam In dentists the mercury is absorbed by breathing the vapor and not through the skin

Mercury fulminate causes a *dermatitis* of the face, neck, hands and forearms, associated with conjunctivitis and inflammation of the nasal and laryngeal mucous membranes The dermatitis is described as moist eczema; the skin is reddened, swollen and tense, later exuding serum, then scaling The eyelids are often much swollen. Hands and forearms are affected first, then face, neck and genitalia A considerable number of

Saita found, in studies of human marrow (sternal puncture) in cases of subacute and chronic plumbism, evidence that the anemia of plumbism has definite characteristics: hyperplasia of the erythroblasts, maturation of erythroblasts and granuloblasts, accelerated in subacute poisoning, delayed in chronic poisoning.

Absorbed lead is deposited in the skeleton as tribasic phosphate which is of low solubility.

Lead ingested in small quantities is excreted in the feces Lead in the urine, *when a person is constantly inhaling lead, reflects the air-lead value in the environ*ment. The deposition and elimination of calcium and hence lead are influenced chiefly by high or low intake of calcium Both acidity and alkalinity of sufficient degree are capable of *dissolving the relatively insoluble tribasic phosphate of lead* deposited in the bone and causing acute exacerbation of symptoms.

SYMPTOMS. Often the first symptom of lead poisoning is pain referable to the joints. *Lead arthralgia* consists of pain in joints or muscles or both of the lower extremities The pain may be severe and accompanied by muscular cramps. There is no swelling of the joints, nor is there tenderness along the course of the nerve trunk.

Lead poisoning may commence with wristdrop The earliest complaint referable to drop wrist is the dropping of the two middle fingers when the hands are stretched out, with fingers separated and extended After drop wrist has been present for two years, it will be permanent Lead is a common cause of peripheral neuritis of many of the peripheral nerves.

The common form of plumbism is manifested by increasing anorexia, disagreeable sweetish taste, dyspepsia, and constipation

Lead colic begins suddenly and is characterized by acute abdominal pain which may be relieved by pressure on the abdomen. Without pressure, however, the pain will subside; *in the interval there is some diffuse abdominal tenderness.* The patient often lies on the face with the fists buried in the midabdomen for relief of the pain There may or may not be vomiting The colic lasts for several days to a week

Lead amblyopia occurs but is a rare manifestation It is the result of an optic neuritis

Lead encephalopathy is preceded by other symptoms of lead poisoning There are headache and disturbed sleep, with increasing irritability and attacks of excitement These symptoms increase until a sudden attack of unconsciousness, with convulsions, or of delirium ensues The attack may begin as a convulsive disorder without warning. Recovery from such an attack is slow, and full recovery is often not attained Permanent mental deterioration, partial or total blindness, and paralysis often ensue

EXAMINATION On examination there is pallor of the skin, out of proportion to the degree of anemia, which is attributed to spasm of the arterioles. There may be a bluish black stippling which appears along the margin of the gums, usually showing most clearly along the lower incisors, but perhaps showing on the buccal surface of the cheeks The stippling lies within the tissues and is composed of the black sulfide of lead produced by contact of the absorbed lead with the hydrogen sulfide produced by the decay of protein matter between the teeth. It therefore is not found in those who take care of their teeth

There is slight extensor weakness of the middle and ring fingers when the hand is held out in pronation If a definite palsy is present, it may involve the extensor muscles of the wrists and fingers, but not the supinator longus or the flexor muscles. At times the deltoid, biceps, brachialis anticus, and the long supinator muscles are weakened. Of the leg muscles the extensors of the toes and foot, the tibialis anticus, may be affected.

There are no specific hematologic changes indicative of lead absorption. Punctate basophilia (or stippling) and reduction in hemoglobin occur *with sufficient*

like that by the trioxide of arsenic, is largely manifested by cutaneous lesions. These lesions vary from a mild inflammation with or without ulceration to scleroderma, melanoderma, warts, and a slowly developing cancer of the skin which usually has a benign course and does not give rise to metastasis

When systemic manifestations occur in the slowly developing arsenical poisoning from solid arsenic, there are neuralgic pains and a mild multiple neuritis with motor palsy. The palsy commonly affects the long extensors of fingers and toes, as does that from lead poisoning.

Lead and calcium arsenate are widely used as spray material for fruits. Thus small quantities of the arsenates of lead and calcium appear in the fruit. Poisoning from eating such fruits does not seem to occur However, poisoning may occur in those who operate the spraying machines if proper caution is not exercised.

Gaseous Compounds of *Arsenic*. When inhaled, arseniuretted hydrogen (hydrogen arsenide, arsine, or AsH_3) causes a rapidly developing, severe form of poisoning.

Arsine is a powerful hemolytic agent. Six to 36 hours or longer, according to the dose, is required after the gas has been inhaled for the destruction of erythrocytes to be manifested. Early symptoms are those of anoxemia, which is followed in 4 to 6 hours by the passage of dark or bloody urine. In 24 to 48 hours jaundice appears As the disease progresses, jaundice deepens and the volume of urine decreases until just before death there is complete suppression Arsenic can always be detected in the urine In those who recover, it may continue to be excreted for many weeks after the acute symptoms have disappeared. The anemia is likely to be chronically persistent.

A cause of poisoning from arsine is the cleansing of tanks and tank cars that have contained either hydrochloric or sulfuric acid There is no danger while the tank is full of the concentrated acid, but when it is emptied and flushed out with water, weak acid is left in the residue The weak impure acid reacts with the iron, and in the reaction arsine forms and accumulates in the tank sludge Anyone entering the tank may succumb to the arsine.

The symptoms of mild arsine poisoning commence some hours after the inhalation of the gas. They consist of headache and nausea More severe poisoning is characterized by exhaustion, dizziness, nausea, pressure in the epigastric region, vomiting, distention of the abdomen, diarrhea, and jaundice, the jaundice appearing in 2 or 3 days after onset of symptoms Paresthesias and neuralgic pains may be present. The urine contains blood and is bile-colored and heavy with albumin.

The diagnosis is suspected from the history of possible exposure.

Hydrogen arsenide poisoning resembles that produced by benzene and its derivatives. It is differentiated from acute poisoning with the nitro and amido derivatives of benzene by the absence of methemoglobin formation and of cyanosis. The presence of jaundice and of blood in the urine favors poisoning with hydrogen arsenide. It has been said that arsine poisoning is the only important industrial poisoning manifested by hemolysis. The hair and the liver of the victim of acute arsenic poisoning contain more arsenic than does the blood or the excreta The arsenic appears late in the hair, five days at the earliest after poisoning, but remains there even longer than in the liver and the bones.

Phosphorus. The inhaled fumes of phosphorus have access to the teeth and thus to the periosteum of the jaw bone. When these fumes are dissolved in the saliva, a solvent action is exerted on the teeth. On continued exposure caries of the teeth result The lower teeth, softened by caries, allow the fumes to penetrate to the periosteum Often fresh sockets from which carious teeth have been extracted admit the fumes to the periosteum

The periosteum and the subperiosteal bone enter into a series of formations of layers of compact tissue and thickening which may persist for several years before necrosis of

cases occur, with nervous symptoms predominating in some, and in others, signs of nephrosis Stomatitis is rare, but salivation and hyperhidrosis may be present.

Mercurialism may arise from the manufacture of tungsten and molybdenum rods and wires for electrical contacts, filaments, electrodes, radio tubes and heaters. Poisoning comes from spillage of quicksilver on wooden benches and floor and from fumes escaping from the apparatus with subsequent contact with the skin while at work.

Organic compounds of mercury used as fungicides affect the *nervous system* and cause tremor, ataxia, dysarthria, and gross constriction of the visual fields but no changes in memory or intelligence.

Mercury compounds are used for treating grain and seed. These compounds volatilize slowly, so that it is not necessary that each seed come in contact with the powder The salts of mercury which are used as fungicides are the acetate, lactate, chloride, nitrate, and borate salts of the phenylmercuric compounds They are used also in the manufacture of some contraceptives and bacteriostatic agents These compounds of mercury give rise to dermatitis

Bichloride of mercury may be accidentally or intentionally ingested. The severe gastrointestinal symptoms caused by the bichloride with nausea, vomiting, pain, purging, and bloody stools and the severe involvement of the kidneys with scanty urine loaded with albumin and casts are unmistakable However, such symptoms are not commonly present in mercurialism unless the exposure is unusually great (see Diseases of the Kidneys, Chapter 11).

On examination of a person who has mercurialism there will be present a fine tremor, worse during volitional movement or under emotional stimulus; irritability, timidity, apprehension, and restlessness; vasomotor disorders, shown by readiness to blush, sweating and dermographia, increased reflexes; gingivitis, and slight abnormalities in speech. Psychic disturbances are detected more often than they are reported by the patients, which is characteristic of this form of intoxication. Instead of dwelling on or exaggerating his trouble, the victim of mercurialism seems anxious to hide it A tendency to underweight, to an increase of systolic blood pressure, and to albuminuria and hematuria are often present.

The diagnosis of mercury poisoning is facilitated by detection of mercury in the organs or body fluids The service of the chemist is required

Arsenic. *Solid Compounds of Arsenic.* Solid white arsenic, the trioxide (As_2O_3), is the compound commonly employed as the killer of pests or of men On ingestion it produces inflammation of the stomach and bowels, violent purging and vomiting, accompanied by a profound nervous collapse, hemolysis with jaundice and scanty bloody urine, and in fatal poisoning, complete suppression of urine As small a dose as 2 grains may be fatal In those who survive, there are sensory nervous disturbance, neuralgic pains, and paresthesias; later there is motor paralysis, together with loss of hair and deformities of the nails.

Other sources of arsenic poisoning may be contact with the white arsenic (arsenic trioxide, As_2O_3) which is added to the glass mixture in the manufacture of glass, contact in stitching window shades that are dyed with arsenic green; and in handling hides and skins treated with white arsenic, as is done by amateur taxidermists.

Poisoning by solid arsenicals when not ingested results from the exposure of the skin to dusts containing arsenic. In this form of poisoning, the skin, mucous membranes and conjunctivae are affected Moist surfaces are affected most, for instance, the lips, nares, eyelids, pharynx and scrotum Hoarseness and perforation of the nasal septum are often present in arsenic workers There is at first a clogging of the nostrils, with consequent mouth breathing, and usually some inflammation in the throat and larynx. There may be salivation much the same as in mercurial poisoning. Sloughing of the mucous membrane and necrosis of the nasal cartilage ensue The bony septum is not involved, and healing occurs without deformity.

Poisoning by copper aceto-arsenite (Paris green), $Cu(C_2H_3O_2)_2\ 3Cu(AsO_2)_2$,

Cadmium food poisoning follows the accidental contamination of acid foods and drinks with soluble cadmium compounds. The source of cadmium in poisoning is from new utensils plated with a plate high in cadmium content. The association of immediate food poisoning of groups with the ingestion of an acid liquid prepared in new metal containers should cause suspicion that cadmium-plated utensils have been used

When a very small amount (67 parts per million) is ingested, symptoms will ensue within 30 minutes, whereas with a larger amount of dissolved cadmium, symptoms appear within 10 to 15 minutes. The symptoms vary from nausea, abdominal cramps, and weakness in persons who have consumed small amounts to vomiting, cramps, and diarrhea in patients who have consumed the large amounts. Thirteen to 15 parts per million of cadmium in popsicles (a fruit beverage frozen in a small mold around a wooden stick, which serves as a handle) will cause violent nausea, but recovery will take place in 5 to 6 hours.

Antimony, Metal Fume Fever, Zinc, and Manganese. *Antimony* resembles arsenic in its action, having an irritating effect on the skin and mucous membranes and causing eczema and other forms of dermatitis and inflammation of the lining of the mouth, nose, and throat It has much less action than arsenic on the nervous system. In other respects, when effects are acute, it resembles lead in causing metallic taste, vomiting, colic and diarrhea, if chronic, indigestion, and loss of appetite and of weight Looseness of the bowels is commoner in antimony poisoning than in lead poisoning Sores in the mouth and sore throat help to distinguish antimony poisoning from that of lead Practically all the antimony of industry contains some arsenic

Printers' type contains more lead than antimony and for this reason it is difficult to differentiate the symptoms of antimonial poisoning among printers from those of lead poisoning because the symptoms of lead poisoning are much the same as those of antimony It is only when a dermatitis is present that the possibility of antimony poisoning is considered.

Antimony food poisoning has resulted from cooking food in gray-enameled cooking utensils of a questionable quality There is a history of the use of new utensils of this kind for cooking of the sickening food The illness is characterized by vomiting within a few minutes to an hour after ingesting the food Recovery is rapid and there is no sequela .

Stibine (antimony hydride, SbH_3) is of the same order of toxicity as arsine Stibine has been shown to be liberated during the "forming" of storage batteries in an acid bath through the action of nascent hydrogen on the antimony present in the plates.

The term *metal fume fever* is used to designate such affections as brass founders' ague, smelter shakes, and brass chills, for the same symptoms occur as those which result from exposure to the hot metallic fumes originating in connection with the use of other metals, especially zinc

The symptoms of metal fume fever come on a few hours after exposure and usually follow chilling of the body The chill is preceded by a feeling of dryness in the throat, with cough and a sense of oppression in the chest The chill is followed by sweating and mild prostration The illness lasts only a few hours. The temperature may reach 101 F (38 3 C) There is leukocytosis which persists for a day or two

Industrial poisoning may be caused by the *zinc oxide* powder which is formed in the smelting of zinc and in brass founding Drinker, Thomason and Finn have shown that a certain degree of resistance may be acquired from repeated exposure. Both zinc chloride and zinc sulfate caustic may cause a troublesome dermatitis. A soluble zinc compound may cause chronic gastritis with vomiting, and the condition does not improve until the exposure to zinc in the air ceases

Manganese is used in the production of steel and the making of dry batteries for flashlights, radios, electric bells and telephones

the bone develops. This process does not go on to necrosis unless there is an injury to the soft parts permitting entrance of pyogenic bacteria. Necrosis follows suppurative inflammation. In rare instances comparable changes occur in the periosteum of other bones, making them brittle and liable to fracture.

In recent years an occasional instance of phosphonecrosis has occurred in phosphorus-producing and converting plants (converting yellow phosphorus into red allotrope) and in the manufacture of phosphor bronze and in making lights for miners' lamps

Acute phosphorus poisoning differs from chronic phosphorus poisoning In acute poisoning there is a vascular collapse from injury of the heart muscle. Fatty degeneration of the liver is common, whereas in chronic poisoning the bone structures, especially the jaw, are affected Salivation, ulcerative stomatitis, and rapid deterioration of the teeth, if there is a possibility of exposure to phosphorus, arouse the suspicion of chronic poisoning

Phosphorus poisoning affecting the jaw is known as phossy jaw because of the swollen, conspicuous prominence of the jaw During the slow, insidious process of development there may not be pain for a long time, but once the tissues are irritated, the pain is intense, prolonged and tiresome, and is accompanied with a foul, fetid discharge and distressing disfigurement.

Radium and radioactive substances cause necrosis of the jaw which resembles that present in phosphorus poisoning.

In acute poisoning of a mild degree there is gastric irritation, nausea, vomiting, and abdominal pain The vomitus smells like phosphorus, is luminous in the dark and may contain blood and mucus Soon a bloody dysentery follows. In severe poisoning the patient may collapse and die in a few hours The patient is lethargic, pale, and ecchymosis of the skin develops The blood pressure decreases rapidly Convulsions may come just before death

In instances of temporary improvement the nausea, vomiting and diarrhea with bloody feces return with renewed violence Evidence and symptoms of hepatic injury are prone to develop, indicated by hemorrhages in the skin or mucous membranes and jaundice. A fully manifested acute yellow atrophy of the liver is common. In some there will be early manifestations of renal injury, oliguria, hematuria and hyperazotemia These manifestations may develop rapidly and end in fatal uremia.

In the diagnosis of acute phosphorus poisoning dependence is placed on the garlicky odor of the vomited material or the feces Luminosity may be present if this material is placed in the dark

Cadmium. Cadmium is used in the manufacture of alloys, bearing metals, and ceramics, in electroplating and process engraving, in cadmium vapor lamps, and for rustproofing tools and other iron and steel articles such as marine hardware. Photoelectric cells, made by coating small steel plates with selenium, are sprayed with metallic cadmium Welding metal or the welding rod may contain cadmium Silver polishes containing cadmium may be the source of poisoning.

Small repeated doses of cadmium cause chronic poisoning, and produce gastroenteritis, emaciation, and infiltration of the liver and heart by fat It is impossible to distinguish these symptoms of cadmium poisoning from those of lead and arsenic In cadmium poisoning there is no colic, but there is pain or tenderness in the epigastrium, associated with nausea and anorexia.

[illegible] when ignited will produce cadmium [illegible] dangerous to those who inhale the [illegible] the eyes, headache, vertigo, dryness of the throat, cough, constriction of the chest and weakness of the legs Ross reported that after 3 hours a set of delayed effects was reported These included complaints of nausea, epigastric pain, dyspnea, precordial constriction, prostration and chills.

is no proof that the ingestion of vegetables or fruits grown on selenious soils adversely affects man.

Selenium poisoning may occur in those engaged in the production of sulfuric acid from iron sulfide carrying selenium sulfide, in the chemical production of hydrogen sulfide, and in copper refineries where selenium is encountered as an impurity. There seem to be, in some men, bronchial irritation, cough, and inflammation of the upper part of the respiratory tract, sometimes pain in the lumbar region, garlic breath, and night sweats It seems, however, that the commonest lesions are dermatitis and paronychia. The teeth may be affected. The hair may become stained red with the precipitation of minute amounts of amorphous selenium in the tissue.

Tellurium. Tellurium compounds are only mildly toxic The possible toxic effects may arise in the recovery of such elements as lead and copper. Tellurium hardens lead and improves its resistance to acids Small amounts of tellurium are used in making chilled car wheels and chilled iron castings, rubber hose and cable coverings. It may be used as a substitute for zinc, nickel, aluminum, magnesium and copper. Alloys of tin, silver, and magnesium are improved by the addition of tellurium.

Steinberg recorded the symptoms of tellurium poisoning as garlic breath, dryness and metallic taste in the mouth, anorexia, nausea, and somnolence. Tellurium was found in the urine in amounts ranging from 0 01 to 0 06 mg per liter of urine. These symptoms were not lasting

Vanadium. The pentoxide of vanadium may cause a suppurating conjunctivitis, inflammation of the upper part of the respiratory tract, cough and profuse expectoration and bronchitis

Aluminum. Aluminum and its compounds are considered harmless in industrial exposures. However, bauxite heated to 3,632 F (2,000 C) gives off fumes which on analysis consist of alumina, silica, iron and magnesium oxides These fumes cause a respiratory disease (Shaver's disease) which is characterized by cough, substernal pain, weakness, and fatigue On roentgenologic examination of the lungs there is bilateral thin shadowing most intense toward the hila of the lungs Distortion of the diaphragm is roentgenographically constant in this disease. The disease may prove to be due to silicosis.

Iron. Ordinary therapeutic doses of soluble iron preparations may produce gastrointestinal symptoms such as an insignificant diarrhea Massive overdosage of iron can produce serious, even fatal, consequences Thus the ingestion by children of 6 0 to 10 0 gm. of ferrous sulfate has produced death with acute hemorrhagic gastritis and hepatic injury Adults can endure large doses of iron.

The parenteral administration of small amounts of iron (colloidal ferric oxide or colloidal ferric hydroxide) may be dangerous It is followed by a febrile reaction, shock and thrombosis of the receiving vein However, there is a preparation of "saccharated iron" which it seems may be administered to patients intravenously in quantities supplying up to 500 mg of elemental iron without development of these toxic reactions

Copper. The green copper sulfate (copperas) is irritating to the skin and the eyes An itching cutaneous eruption may arise from contact with finely divided "cement copper" obtained from the precipitation of the metal from solution by metallic iron On exposure there may be irritation of the nasal passages and the throat, and a sweetish taste in the mouth Copper when imbedded in the skin or in the eye gives a rather violent inflammatory reaction Copper sulfate when ingested produces gastrointestinal irritation, vomiting and severe diarrhea.

Tin. The only use of tin in industry which causes injury seems to result from the use of tetrachloride of tin in weighting silk.

Tin poisoning is practically unknown Most of the reported outbreaks of food poisoning reputedly traced to tin date back many years, and these outbreaks were probably due to other causes.

Manganese poisoning may be manifested as a psychic type of intoxication or as a parkinsonian or extrapyramidal neuron type of nervous manifestation. The psychic symptoms of manganese poisoning are impulsive acts, running, dancing, singing and uncontrolled talking Some patients have attacks of irritability. The nervous symptoms comprise the presence of tremors, a parkinsonian masked expression, muscular pains, and hoarse dysarthric voice The prognosis is generally good but recovery is slow Some may die

Beryllium and Berylliosis. Beryllium and beryllium compounds have many uses in combination with copper, aluminum, nickel, magnesium, silver and iron Beryllium is employed as a phosphor in the manufacture of fluorescent lamps, radio and electronic tubes, neon sign tubing, incandescent lamps, electric heating elements, roentgen ray tube windows, and luminous indicators. *Beryllium oxide* is used as a refractory in certain types of crucibles and in bricks for high temperature ovens.

The toxic effect appears to be due to the vapors of beryllium oxyfluoride in a state of great dispersion. Vapor dispersion also explains the occurrence of poisoning of workers at a distance from the source of vapors

The clinical manifestations of acute berylliosis caused by fumes are characterized by two stages The first stage consists of the symptoms of metal fume fever. The second stage begins 1 to 4 or more days after the metal fume fever and is characterized by an extensive pneumonitis with a tendency for relapses. The relapses are characterized by severe dyspnea, cyanosis, paroxysmal cough, blood-streaked sputum and high fever The pneumonitis clears in from 1 to 4 months.

Hardy and Tabershaw in 1946 called attention to "delayed chemical pneumonitis" in workers exposed to beryllium The entity they described is characterized by a delay between exposure and onset of illness of from 3 months to 3 years A delay of 5 years has been observed

Microscopic studies revealed a granulomatosis Studies of sputa and of sections of lung did not reveal pathologic bacteria.

The manifestations are the same as those present in the second stage of the acute form of poisoning The disease progresses despite change of environment. There is a progressive loss of body weight On roentgenologic examination the roentgenograms reveal a diffuse nodulation throughout the lungs which resembles that occurring in miliary tuberculosis and silicosis These changes are incident to a pulmonary granulomatosis due to the inhalation of the fumes of beryllium.

The term *berylliosis* designates a granulomatosis of the lungs, more rarely of the skin, subcutaneous tissue, lymph nodes, liver, and other structures A berylliosis may be caused by inhaling or by accidentally implanting finely divided beryllium dust in the skin or subcutaneous tissue by laceration or puncture

In berylliosis fine particles of beryllium may be found in cutaneous papules, in cutaneous ulcers, and in granulomas.

Beryllium granuloma is a specific process, as illustrated by Nachtwey's case The patient, a man aged 35 years, was in the electric business and had worked with fluorescent lamps, blowing the glass and coating the tubes. For many years he had a nonproductive cough and more recently he had noticed dyspnea, fatigue, and thoracic pain. Examination revealed persistent fine rales over the lower two thirds of both pulmonary fields. At the base of the nail on the left fourth finger there was a healed scar, which the patient said was the result of a lesion which would occasionally swell, drain and then heal over He thought this lesion had followed a cut by a piece of fluorescent glass. An abnormally enlarged lymph node was found in the left axillary space. This node was removed; microscopic examination revealed that it was a granuloma, and spectrographic analysis disclosed beryllium

Selenium. Cattle that feed on grass grown on certain alkaline soils containing excessive amounts of selenium have what is known as alkali disease. However, there

most effective against arsenical poisoning and has proved of practical value in preventing and counteracting many of the toxic effects of antisyphilitic arsenicals.

The administration of BAL causes lead to appear in the urine in increasing quantity with only a slight exacerbation of symptoms of plumbism The untoward symptoms from the administration of BAL in man are a feeling of constriction and oppression in the chest, burning lips, dry throat, nervousness and restlessness, nausea and vomiting. There may be a transient rise in blood pressure.

Carbon Monoxide. Carbon monoxide gas is odorless, tasteless and nonirritating. Carbon monoxide is formed whenever there is incomplete combustion of carbon. Natural gas does not contain carbon monoxide, but unless it is burned with sufficient supply of oxygen the vapors which form during its combustion may be very rich in this substance. Other gases which are used for illumination and for heat and power contain varying amounts of carbon monoxide, and the gases that result from the explosion of coal dust, from the detonation of blasting charges, and from the partial burning of such charges may contain carbon monoxide in detectable to sizable concentrations

When there is a concentration of about 0 02 per cent of carbon monoxide in the inspired air, discomfort begins

Truck drivers, occupants of cars with faulty exhaust systems, and traffic policemen may complain of malaise and mild headaches If the carbon monoxide is excessive, the occupants of cars after a 3 or 4 hour run have collapsed from carbon monoxide asphyxia

In any place where carbon monoxide gas is used as a source of heat or power, or in the production of illuminating gas and of power gas, or in the repair work on pipes or when the pipes and flues are cleaned, there is some danger of excessive amounts of this gas being present

Carbon monoxide acts more quickly at high temperatures, in humidity, and during muscular exertion than under other conditions Young persons are more susceptible than older ones Those who have chronic bronchitis or asthma, alcoholism, obesity, and chronic disease of the heart are the most susceptible to the effects of carbon monoxide.

The asphyxia of carbon monoxide is due to an increased affinity of hemoglobin for this gas and the more stable compound, carbon monoxide hemoglobin, formed when hemoglobin is combined with it In addition, carbon monoxide hemoglobin in the blood interferes with the dissociation of the oxyhemoglobin For instance, a person who has anemia and who has lost one half of the total blood utilizes the oxygen in the blood well enough to be fairly comfortable, whereas a person who has one half of the blood saturated with carbon monoxide hemoglobin is not comfortable

The lesions in the central nervous system are primarily vascular. A hyperemia of the cerebral tissues seems to be the first effect of the anoxemia There is a rise in intracranial blood pressure attributable to the increased congestion and edema The congestion of the brain is as intense as that observed after strangulation or drowning.

The cell degeneration, necrosis, and subsequent softening vary in intensity according to the adequacy or inadequacy of the blood supply, and are typically most marked in the lenticular nucleus of the corpus striatum, particularly the pallidal region The exaggeration of the process in the globus pallidus of the lenticular nucleus is explained by the poor blood supply This degeneration may proceed in those who recover, apparently, and who have been adequately treated

Hemorrhage may occur in practically every organ or tissue as a result of the high blood pressure and of the dilatation and weakening of the vessel walls. There may be epistaxis and hemorrhage from both nose and lungs, from the uterus with premature expulsion of [illegible]
culature of

The inh

There is a common concept among the laity that food may become poisonous if it is left standing in an open tin can. Poisonous effects or spoilage results from bacteria growing in a food and not from the tin can Contamination is less likely to occur if the food is left in the sterile can than if placed in a clean but not sterile dish.

Nickel. Nickel eczema or "nickel itch" seems to be fairly common in those who work in nickel-plating plants The eczema comes first on the arms and may spread to the neck, the legs, or the body. There are itching, soreness and burning, and sometimes swelling of the parts affected. Nickel seems to be a true allergen.

Nickel carbonyl is a gaseous compound of nickel which volatilizes at room temperature, and when heated to 302 F (150 C), decomposes with a deposit of metallic nickel and the release of carbon monoxide.

Nickel carbonyl is decomposed in the lungs into carbon monoxide and some gaseous compound of nickel The gaseous nickel compound in the lungs produces congestion, edema, and consolidation which may be fatal. Once the gaseous compound is in the blood, the endothelium of the capillary vessels is injured and hemorrhages, especially in the brain and the adrenal glands, ensue.

Magnesium. Wounds, scratches, or cuts that are caused or contaminated by magnesium or its alloys are prone to become inflamed, with accompanying blebs which resist healing. All particulate magnesium should be removed from a wound

Thallium. Thallium poisoning follows the use of the metal as a depilatory, in the treatment of parasitic diseases of the hair follicles, in children especially, or its administration, in the form of a rat exterminator, for murder or for suicide. Thallium is a powerful agent for the removal of hair It will cause complete loss of hair in children on the sixteenth to eighteenth day Poisoning has followed such administrations of thallium Toxic effects are manifested by swelling of feet and legs, with pains in the joints sometimes suggestive of acute articular rheumatism, hyperesthesia and paresthesia of hands and feet, colic and vomiting, and sleeplessness and mental confusion. It is possible to demonstrate thallium in the blood and urine 4 weeks after the administration of a large dose.

Industrial thallium poisoning is characterized by coloration and subsequent falling out of the hair, severe cramplike pains in the knees and calves; and optic neuritis, followed by atrophy

Cobalt. A lack of cobalt in the soil may produce a deficiency disease in sheep and cattle. No such disease is recorded in man The powdered cobalt encountered in the tungsten-carbide industry will cause dermatitis in man Arsenical compounds of cobalt may cause a localized dermatitis Cobalt is eliminated from the tissues slowly.

Platinum. Complex platinum salts are encountered in photography Karasek and Karasek have described a specific clinical syndrome due to platinum poisoning which is characterized by sneezing and respiratory distress.

Osmium. Osmium produces an exceptionally hard alloy, used to tip fountain pens, as a catalyst in preparing synthetic ammonia, in taking fingerprints, and in the laboratory technics of histology. Osmium causes lacrimation and pain and irritation of the eyes.

The inhalation of osmium tetroxide has a marked and immediate effect on the mucous membranes of the nose, throat, and bronchi with a sensation of constriction of the chest and inability to breathe which is of short duration.

Silver. Argyria, a bluish black deposit of metallic silver in the skin, apparently is the only lesion produced by silver It is localized usually in those areas of the skin which have come in contact with silver. The condition appears slowly, taking from 2 to 25 years or even longer to develop There may be pigmentation of the lining of the mouth Argyria, local or generalized from prolonged application or ingestion of silver-containing medicaments, is now very infrequent.

BAL. The use of BAL (British anti-lewisite), 2, 3-dimercapto-1-propanol, as an antidote for metallic poisons has come to be a common remedy. It seems to be the

Asphyxiation with cyanide gas occurs in connection with the fumigation of ships, workshops, and dwellings, in fumigation intended to kill agricultural parasites, in chemical laboratories, in blast-furnace gas, in the manufacture of illuminating gas, and in the gas from burning nitrocellulose, in the preparation and decomposition of cyanides by exposure to the air and by weak acids; in the extraction of phosphoric acid from bones; and in the use of lime from gas works in tanneries as a tanning agent. Hydrogen cyanide is produced in nature by certain plants as a side reaction in their protein metabolism with occasional accidental poisoning to agricultural workers and animals.

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Hydrogen Sulfide During the separation and deposition of free sulfur in nature, pockets of hydrogen sulfide may accumulate. For instance, hydrogen sulfide may collect in pools of water in coal mines when iron pyrites decompose, in waters from industrial plants, and where the somatic decay of man and animals occurs. Gassing from hydrogen sulfide occurs in tanneries, glue factories, fur-dressing and felt-making plants, abattoirs, beet-sugar factories and sewers Hydrogen sulfide is formed in certain industrial processes, as in the production of sulfur dyes, brown, black and blue; production of carbon disulfide, in the action of acids on sulfides, in purifying sulfuric acid; in heating rubber containing certain sulfur compounds in the process of vulcanizing.

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Mild forms of hydrogen sulfide poisoning are characterized by irritation of the conjunctivae and sometimes by a severe conjunctivitis with keratitis. If aware of the significance of an increased sensitiveness to all kinds of light and the appearance of a colored ring around a light, a person exposed to hydrogen sulfide may escape serious poisoning. In more severe poisoning the eyelids become swollen. So great may be the swelling that both the upper and lower lids are everted

Recovery from acute poisoning by hydrogen sulfide is usually complete, but on rare occasions lasting injury, which is irreversible, in certain cells of the body results in prolonged anoxia and thus permanent injury. Permanent injury from hydrogen sulfide is manifested much the same as that from hydrogen cyanide and carbon monoxide.

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body temperature, and in fatal gassing there is a fall in the oxygen content and the carbon dioxide content of the blood, together with an increase in blood sugar. The hydrogen ion concentration of blood is lowered

Administration of alkalies lessens the injury from carbon monoxide and decreases the concentration of blood sugar

The symptoms of acute carbon monoxide poisoning are described in stages In the *first stage* there may be no awareness of the impending disaster. In some, however, there may be a sense of pressure in the head or bandlike constriction or throbbing, a feeling of weakness in the knees, mental confusion, headache, roaring in the ears, nausea, and perhaps vomiting.

On continued exposure the *second stage* of poisoning commences with headache, dizziness, and inability to think clearly and to decide and act Soon the victim becomes soothed to drowsiness and thus fearless Soon consciousness is lost, which is attended by vomiting and involuntary evacuations, and occasionally general muscular contractions Rarely are there convulsions until just prior to death, convulsions may appear with the return to consciousness if the patient has been rescued and is undergoing treatment

The presence of abnormal amounts of moisture in the lungs is a common manifestation of acute gassing The moisture may increase until edema of the lungs ensues Pneumonia, often deglutitive in origin because the patient may have vomited before recovering consciousness, often develops. A pneumonia may occur weeks after the accident as the result of lowered resistance to infection.

In severe gassing, when consciousness is regained, there is excitement, often delirium, with an ensuing depression, apathy, indifference to the surroundings, shivering, and inability to remember anything about the accident. Convulsive disorders or psychoses may appear for the first time during recovery.

Blindness, complete or incomplete, transient or permanent, is a rare accompaniment or a sequel of carbon monoxide asphyxia.

On examination the appearance of the victim is unforgettable. The cheeks and lips are richly pink in color, and there are red blotches on various parts of the skin. If consciousness is still maintained, there are manifestations comparable to those present in alcoholic intoxication. Later the red blotches over the skin may form blisters, and trophic changes, necrosis and gangrene ensue.

Carbon monoxide in excessive amounts may be demonstrated in the blood by chemical or spectroscopic analysis A profound anemia often develops

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Carbon Dioxide. Carbon dioxide poisoning is rare When it does occur, it is from gas produced by the fermentation of carbohydrates Green fodder in silos and residue in brewery vats have caused fatal poisoning Carbon dioxide may also be a danger in beet-sugar production, since the juice of the beets is treated with milk of lime and the calcium saccharate is precipitated by carbon dioxide The handling of dry ice, or carbon dioxide snow, solid carbon dioxide, causes injury to the skin.

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ALLERGIC REACTIONS TO DRUGS AND CHEMICALS

Drugs and *chemicals* are common sources for hypersensitiveness. These agents are sources of drug idiosyncrasy as well as the ill effects from unknown and unpredictable physiologic action Often it is impossible to determine whether symptoms are of allergic origin or whether they are due to the physiologic action of the drug Likewise it may be impossible to learn whether the hypersensitiveness was produced by contact or by ingestion.

Generally, when there is hypersensitiveness to a drug or chemical, the compound is of low molecular weight, for instance the frequency of response to formaldehyde, *2, 4-dinitro-1-chlorobenzene*, paraphenylenediamine, mustard gas, quinine, aminopyrine, sulfadiazine, and metals such as nickel

When due account is taken of all the tangible factors, such as age and weight, which might alter the susceptibility of persons to drugs, there still remains a wide normal variability in the quantitative response Pharmacologists take cognizance of this by the use of such terms as ED_{50}, ED_{99} and ED_1, signifying by the first the average dose of a drug which is effective in 50 per cent of the population and using the latter two terms to give expression to the range of variability by indicating the doses which are correspondingly effective in 99 per cent and 1 per cent of the population Persons showing susceptibilities at or beyond these extremes are said to be tolerant in the former and hypersensitive in the latter case The quantitative variability in the response to drugs is not particularly disturbing in clinical practice and seldom precludes the use of any drug Largely because of this fact, the term idiosyncrasy has come to have the narrower meaning of a qualitative abnormality in the response to drugs, signifying such effects as urticaria, neuritis, jaundice, anemia, leukopenia and the like, which some drugs produce in some persons but do not produce in the majority, irrespective of the dose employed Whether idiosyncrasy is due to a constitutional defect, unchangeable and incurable, or to a transitory state brought about by disease or nutritional deficiency is not known The statement is commonly made that some 10 per cent of the population have an inherited predisposition to the allergic diseases caused by foods, inhalants and similar environmental agents Whether this is the same fraction of the population that shows idiosyncrasy to drugs is not known.

The causative agents in drug allergies and contact dermatitis are not antigens, but it appears that by combining the offending agent with the tissues of the host, the tissues acquire antigenic capacity and function which arise when hapten structures become attached to indifferent foreign protein

The cutaneous lesions from a drug depend on the method of exposure to the drug. These eruptions may arise as a consequence of contact of the drug with the skin or as a consequence of ingestion of the drug.

The manifestations of allergy to drugs may be anaphylactic, immediate-type [illegible] example, *like those of serum sickness*, arthralgia, [illegible] asthma, flare-and-wheal reactions, urticaria, [illegible] by far the most commonly encountered is the delayed type Aside from an inherited predisposition in a given person, the chief determining elements appear to be the frequency and mode of contact through which sensitization has arisen and especially the chemical properties of the sensitizing material.

Common offenders among drugs are aspirin, salicylates, phenacetin (acetophenetidin), *iodides, bromides, sulfonamides, penicillin,* phenolphthalein and ovarian extracts. The heavy metals, among them arsenic (inorganic and organic compounds), gold, silver, lead and bismuth produce erythema, papules, vesicles and ulcerations Gold, silver and bismuth are all dangerous to the skin Silver may

stain the skin a dark bluish color which is permanent (argyria). Bismuth and mercury cause stomatitis (salivation).

In any instance of a sudden appearance of a cutaneous rash all medications being used at the time are suspected as the cause of the eruption, irrespective of the length of time the drug or drugs have been administered One or two doses of a drug may be sufficient to produce an eruption. The eruption occurring from ingestion of the drug seems to arise most commonly in persons who have a decreased renal functional activity or in those who have a congenital or acquired sensitiveness to the drug in use

Dermatosis and Dermatitis Due to Chemical Agents. Many and varied forms of dermatosis arise from drugs, toilet articles (soaps, perfumes, talcum powders, cold creams, nail polishes, hair dressings, hair waving preparations) and contact with plants. Most of these are described in appropriate places in this text.

DIAGNOSIS OF POISONING BY CHEMICALS

The diagnosis of a disease due to a chemical agent requires a history of a contact or a suspicion of its nature, or manifestations specifically indicating a particular poison. In the absence of such information the special technics of qualitative and quantitative chemical analysis are so limited that the number of procedures necessary to identify an unknown agent would occupy the lifetime of the chemist. It is for these reasons that the emphasis in the descriptions of the chemical agents of disease is placed on contacts and the possible sources of contacts with these agents, organic or inorganic

ACUTE POISONING BY CHEMICALS WHICH REQUIRES IMMEDIATE TREATMENT

Acute emergencies arise from the accidental or intentional ingestion, inhalation, or absorption of certain chemicals In such instances the diagnosis of the offending substance may be obvious or totally obscure, depending on the circumstances When suicide is the intent, the patient usually lives long enough to repent. However, when homicide is the intent, there is no immediate information at hand in regard to the chemical or its method of administration. In any case, immediate treatment is urgent

In instances of poisoning when there is no evidence available as to the nature of the offending agent, and even if such information is at hand, there are three approved therapeutic procedures, one or more of which may be employed, depending on the situations which prevail These procedures are (1) gastric lavage, (2) emetics and (3) antidotes Antidotes are of two kinds (a) those which seem to be safe and which usually are beneficial and (b) specific antidotes. The specific antidotes themselves are poisons and their administration is limited by their own range of safe dosage

Gastric Lavage. In infants the gastric tube is introduced through the mouth. However, a small tube (No 8 to No 10 French catheter) may be introduced through the nose Solutions generally used in lavage are water, saline, weak sodium bicarbonate, potassium permanganate 1.10,000 solution, specific or general antidotes, and cathartics It is well to remember that compounds formed by antidotes may be only slightly less toxic than the poison itself. All chemical antidotes, stimulants, or sedatives are employed cautiously and if there is doubt, they are not used at all Avoid saline cathartics in phosphorus poisoning, and the passage of stomach tubes when caustics have been the offending agents.

The contraindications to lavage are (1) strychnine poisoning in which the characteristic muscular spasms may be changed, by the stimulating effect of gastric

lavage, to fatal convulsions; (2) erosion of the esophagus due to corrosive agents such as phenol (the tube may cause perforation of the esophagus); and (3) shock, if shock supervenes. If shock should be present, its treatment takes precedence over lavage. The therapy is by inhalation of oxygen with 5 per cent carbon dioxide. Artificial respiration is instituted in instances of depressed respirations.

The general precautions during lavage are as follows: (1) restrain the patient, (2) turn the head to the side and keep it low in order to prevent aspiration into lungs, (3) use amounts of liquid just sufficient to be aspirated by suction with a large glass syringe and (4) close the tube by pinching it before withdrawing from the stomach.

Emetics. In general, emetics are not used to avoid the employment of gastric lavage However, many lives are saved by the voluntary or involuntary induction of vomiting, which is often an efficient way of emptying the stomach It is only in rare instances that emetic drugs are of value. Emetics are avoided if strong acids or alkalies have been ingested If the situation demands the psychologic effects of an emetic, harmless ones consist of (1) 2 tablespoonfuls of salt in 1 glass of warm water or milk, (2) ¼ glassful of a mild soapy water solution, (3) 1 teaspoonful of dry mustard in 1 glass of warm water Any one of these emetics may be administered at 15-minute intervals until vomiting ensues.

Antidotes. ***Unknown Poisons.*** If after gastric lavage the poison is unknown, an antidote consisting of powdered charcoal, 2 parts; magnesium oxide, 1 part; and tannic acid, 1 part, is given The dose is 1 teaspoonful in a small glass of lukewarm water Simple home remedies may be useful. (1) flour and starches for their colloidal action on iodine, (2) weak tannic acid, strong tea or dilute tincture of iodine (10 drops in ½ glass of water) is effective against alkaloids such as atropine or morphine, (3) milk and eggs are useful in heavy-metal poisoning for they provide protein to precipitate these metals, (4) strong coffee or tea is valuable as a stimulant when the central nervous system is depressed, as occurs when excessive doses of opiates, barbiturates or alcohol have been consumed.

Known Poisons. In the next few pages are discussed antidotes for use when the poisons are known.

Acetic Acid, Chromic Acid, Hydrochloric Acid, Nitric Acid, and Sulfuric Acid The lethal dose of acetic acid is up to 20 ml; of nitric acid, 6 to 8 ml., of sulfuric acid, 4 to 6 ml

The patient should drink freely of lukewarm water until vomiting ensues Magnesium oxide, chalk or soapy water or other protective substances such as eggs are administered after vomiting but never in excessive doses (1 glassful each half hour) For acid vapor inhalation the nose should be sprayed and the mouth washed with a solution of sodium bicarbonate

Alcohol. The lethal dose is undetermined. The stomach is washed with water. Heat is applied to the body, cold applications are applied to the head, and black coffee is given freely (see Alcohols, p. 1402) If delirium is present, barbital is administered intravenously as pentobarbital sodium, 0 25 to 0 40 gm

Alkalies, Caustic Soda, Liquor Potassae The lethal dose is about 150 to 300 grains. Injuries due to ingested alkali are treated by the use of weak acids such as vinegar water, sour wine, tartaric acid, citric acid, lemon juice or apple juice and milk. Washing of the stomach with acidulated water (a teaspoonful of vinegar to 500 ml water) may be used, but with caution. For alkali in the eye, water is used to wash the eye and is sprayed under the lids with a medicine dropper, if available If a dropper is not available, hold the upper lid up and wash For lime in the eye 0 10 per cent sulfuric acid solution (1 teaspoonful to 1,000 ml) may be used as a wash, but with great caution.

Ammonia. The lethal dose of caustic ammonia solution is *1 ounce. When the* esophagus and stomach are eroded, the treatment is the same as for injury from

ı the air passages have been injured, the inhalation of the vapor
/inegar or lemon juice may be helpful.
ıvatives. Acetanilid, nitrobenzol, antipyrine, phenacetin, dichlori-
nol are aniline derivatives. The lethal dose of aniline is less than
id and of nitrobenzol, 64 to 160 grains.
avaged and charcoal administered if shock or depressed respira-
If these are present, artificial respiration, oxygen inhalation, and
re employed When nitrobenzol is the poison, oily or alcoholic
dministered. The patient is removed to a cool darkened room.
ımonial Wine and Tartar Emetic) The lethal dose is 50 grains.
aged and immediately afterward tea and magnesium oxide or
instilled
tion of the stomach is done, and if cysteine is available, 100 mg
amuscularly per kilogram of body weight Parenteral fluids are
red.
ous acid, Fowler's solution, sodium arsenate, sodium cacodylate,
salts, Donovan's solution, fly paper and fly stone may contain
lose of arsenic trioxide is 1⅔ to 3⅓ grains
stomach with a solution of sodium bicarbonate is performed If
n of BAL (10 per cent in peanut oil) should be used in the
ıtramuscularly If BAL is used, reactions to it are at least par-
: intramuscular or oral administration of 25 mg ephedrine sulfate
n Morphine is employed for the pain The intravenous adminis-
ıc saline solution may be required to correct fluid and electrolyte

donna, Stramonium and Scopolamine. The lethal dose of atropine
elladonna, 3 to 10 berries, 50 mg. of extract (5 to 10 ml. of
ıonium, 100 seeds (10 ml of tincture); of scopolamine and
han 1 grain
prises emptying the stomach by means of lavage, and thereafter
Ice Cold sponges to the skin are valuable. Opiates or physostig-
:d as indicated by the prevailing conditions
arbiturates depress the medullary centers, and the chief cause of
ratory failure However, death may occur later from aspiration

ısoning produces a deep sleep followed by coma with decreasing
ratory depression, and eventually loss of all reflexes. The pupils
or dilated
ırway must be established and maintained Oxygen under pres-
:d If necessary, intratracheal intubation by a trained anesthetist
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External heat is of value therapeutically.
e physician sees the patient, lavage will usually be of little value.
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ry edema hypertonic glucose solutions may be helpful to induce
: valuable analeptics are metrazol and picrotoxin
apparent complete cessation of respiration with continued cardiac
may be benefited by the use of metrazol The dose of metrazol
:gree of depression and should be sufficient to arouse the patient
peated often enough to keep the patient conscious. In cases of
5 to 6 ml of metrazol intravenously is a safe first dose followed
10 ml. unless reflexes return. If ...

lavage, to fatal convulsions; (2) erosion of the esophagus due to corrosive agents such as phenol (the tube may cause perforation of the esophagus); and (3) shock, if shock supervenes. If shock should be present, its treatment takes precedence over lavage. The therapy is by inhalation of oxygen with 5 per cent carbon dioxide. Artificial respiration is instituted in instances of depressed respirations

The general precautions during lavage are as follows: (1) restrain the patient, (2) turn the head to the side and keep it low in order to prevent aspiration into lungs, (3) use amounts of liquid just sufficient to be aspirated by suction with a large glass syringe and (4) close the tube by pinching it before withdrawing from the stomach.

Emetics. In general, emetics are not used to avoid the employment of gastric lavage However, many lives are saved by the voluntary or involuntary induction of vomiting, which is often an efficient way of emptying the stomach. It is only in rare instances that emetic drugs are of value. Emetics are avoided if strong acids or alkalies have been ingested. If the situation demands the psychologic effects of an emetic, harmless ones consist of (1) 2 tablespoonfuls of salt in 1 glass of warm water or milk, (2) ¼ glassful of a mild soapy water solution, (3) 1 teaspoonful of dry mustard in 1 glass of warm water Any one of these emetics may be administered at 15-minute intervals until vomiting ensues.

Antidotes. *Unknown Poisons.* If after gastric lavage the poison is unknown, an antidote consisting of powdered charcoal, 2 parts; magnesium oxide, 1 part; and tannic acid, 1 part, is given. The dose is 1 teaspoonful in a small glass of lukewarm water. Simple home remedies may be useful: (1) flour and starches for their colloidal action on iodine, (2) weak tannic acid, strong tea or dilute tincture of iodine (10 drops in ½ glass of water) is effective against alkaloids such as atropine or morphine, (3) milk and eggs are useful in heavy-metal poisoning for they provide protein to precipitate these metals, (4) strong coffee or tea is valuable as a stimulant when the central nervous system is depressed, as occurs when excessive doses of opiates, barbiturates or alcohol have been consumed.

Known Poisons. In the next few pages are discussed antidotes for use when the poisons are known.

Acetic Acid, Chromic Acid, Hydrochloric Acid, Nitric Acid, and Sulfuric Acid. The lethal dose of acetic acid is up to 20 ml ; of nitric acid, 6 to 8 ml.; of sulfuric acid, 4 to 6 ml

The patient should drink freely of lukewarm water until vomiting ensues Magnesium oxide, chalk or soapy water or other protective substances such as eggs are administered after vomiting but never in excessive doses (1 glassful each half hour) For acid vapor inhalation the nose should be sprayed and the mouth washed with a solution of sodium bicarbonate

Alcohol. The lethal dose is undetermined. The stomach is washed with water Heat is applied to the body, cold applications are applied to the head, and black coffee is given freely (see Alcohols, p 1402). If delirium is present, barbital is administered intravenously as pentobarbital sodium, 0 25 to 0.40 gm.

Alkalies, Caustic Soda, Liquor Potassae. The lethal dose is about 150 to 300 grains Injuries due to ingested alkali are treated by the use of weak acids such as vinegar water, sour wine, tartaric acid, citric acid, lemon juice or apple juice and milk. Washing of the stomach with acidulated water (a teaspoonful of vinegar to 500 ml. water) may be used, but with caution For alkali in the eye, water is used [illegible] with a medicine dropper, if available. [illegible] lid up and wash. For lime in the eye [illegible] onful to 1,000 ml.) may be used as a wash, but with great caution.

Ammonia The lethal dose of caustic ammonia solution is 1 ounce. When the esophagus and stomach are eroded, the treatment is the same as for injury from

Colchicine. The lethal dose is 1/3 grain The stomach is emptied, and milk or 2
[illegible] may be necessary
[illegible] 'thal dose is 150 to 300 grains. Gastric lavage
[illegible] tash (1:1,000 solution) is performed After the lavage, albumin of 1 egg is instilled into the stomach and a comparable dosage of egg albumin is given each 4 hours The oral administration of magnesium oxide, potassium iodide and charcoal is a valuable treatment

Croton Oil. Administer mucilaginous and oily substances. Opiates may be necessary to allay tenesmus from frequent bowel movements.

Crude Petroleum. See Benzene Poisoning, page 1396.

Cyanide. The lethal dose of hydrocyanic acid is 1 grain, the lethal dose of potassium cyanide is 3½ grains If cyanide is swallowed, apomorphine (5 mg) is administered subcutaneously unless muscular cramps are present. After the patient has vomited, gastric lavage with 1 2,000 solution of potassium permanganate or 2 per cent solution of hydrogen peroxide and charcoal is performed Methylene blue, 50 ml., administered intravenously, followed by intravenous injection of 50 ml. of a 2 per cent solution of sodium hyposulfite, given slowly, may be used in all instances of poisoning with this chemical The administration of 20 units of insulin may be helpful. Artificial respiration (with oxygen) is used if necessary and if time permits.

If cyanide is inhaled, emetics and washing out the stomach are not helpful.

DDT. The stomach is lavaged with warm water. Five to 10 ml of a 10 per cent solution of calcium gluconate may be given intravenously. If convulsions occur, atropine and barbiturates may counteract them Glucose may be administered orally or parenterally if sufficient fluids cannot be taken by mouth. (See DDT Poisoning, p 1412.)

Digitalis The lethal dose of digitalis varies through wide limits. Forty to 50 grains of the leaves or 1 ounce of the tincture are considered lethal. The stomach is lavaged, and atropine, alcohol, tea, and coffee may be administered Often death can be prevented if physical effort is avoided. If necessary to procure absolute rest, the patient, including the arms and legs, may be wrapped tightly in a blanket or a bed sheet

Ephedrine Immediate gastric lavage is performed and sedatives are administered.

Ergot (Secale cornutum, Aconite) The lethal dose is 16 to 64 grains of ergotamine. Gastric lavage is performed immediately Opiates, amyl nitrite or nitroglycerin may be administered in adequate doses

Formaldehyde (Formalin) The lethal dose is 1 ounce of the 4 to 40 per cent solution Immediate gastric lavage, followed by the administration of 6 raw eggs, should be performed Administration of urea in doses of 20 grains may be repeated. Cutaneous injuries may be washed with dilute ammonia or ammonium carbonate When the poison is in the eye, treatment with weak ammonia vapors is safe.

Insulin Insulin shock is treated by the immediate administration of fruit juices of any kind by mouth If the patient is unable to take liquids by mouth, 20 ml. of a 10 per cent solution of dextrose is given intravenously. If shock is severe, 0.5 ml of 1.1,000 epinephrine solution subcutaneously may precede the administration of the dextrose.

Iodine, Iodoform, Tincture of Iodine The lethal dose of iodine is 48 to 64 grains; of iodoform, 128 grains; of tincture of iodine, ⅔ to 1 ounce. Immediate gastric lavage is performed and is followed by the instillation into the stomach of a solution of starch or of a solution of sodium bicarbonate.

Iron Large amounts of iron are required to kill The stomach should be lavaged with generous amounts of warm water followed by the administration of milk and egg albumin

every 30 minutes may be given until reflexes return. Thereafter small doses intramuscularly should be used until full consciousness is restored.

Picrotoxin is used in doses of 1 to 3 mg. dissolved in physiologic saline solution and administered slowly intravenously. Picrotoxin should not be given if there is a weak heart or pulmonary edema.

Caffeine is not nearly so effective a respiratory stimulant as metrazol but may be used if necessary, as caffeine-sodium benzoate administered subcutaneously.

Barium Chloride and Barium Nitrate. The lethal dose of barium chloride is 48 grains; of barium nitrate, 48 to 64 grains Gastric lavage with a solution of sodium sulfate (500 grains to a quart of water) is employed. Milk, albumin or tannin may be left in the stomach after lavage.

Benzine, Benzol and Kerosene Benzine is a distillate from petroleum, whereas benzene is a distillate of coal tar The lethal dose of benzine is about the same as of benzene, ⅓ to 1 ounce (see Benzene Poisoning, p 1396), of benzol, 1 ounce. In acute poisoning with benzine or benzol the stomach is lavaged with tea, and cardiac stimulants are administered if necessary. For kerosene poisoning, see Petroleum, page 1399

Bismuth The symptoms and treatment are the same as those of mercury poisoning

Boric Acid The stomach may be lavaged with a solution of sodium bicarbonate if the boric acid has been taken orally Sodium lactate may be administered to correct acidosis. Parenteral administration of chlorides to counteract displacement of boron in body fluids is valuable treatment. (See also Boric Acid Poisoning, p 1418.)

Bromides. Gastric lavage is done if the patient is seen immediately after ingestion of the drug If not, caffeine is given subcutaneously and sodium chloride, a 1 per cent solution, is administered intravenously (see Bromide Intoxication, p 1417).

Calabar Bean Gastric lavage is used if the patient is seen early after ingestion of the beans Atropine is an antagonist to the action of calabar beans and should be given hypodermically until the pupils dilate. Strychnine hypodermically, strong coffee and brandy orally, and artificial respiration are appropriate measures as the occasions arise for their use

Cantharides. After the stomach is emptied, mucilage of acacia is given to soothe; anything fatty or oily is avoided until gastric irritation has subsided

Carbolic Acid The lethal doses by mouth of phenol, lysol, and compound cresol solutions are ¼ to ½ ounce Emetics, lime water, magnesium sulfate, magnesium oxide and milk, are administered. Stimulants may be necessary immediately. Later in the illness opiates may be necessary for the pain

Carbon Monoxide Illuminating gas, trench gas and carbonic acid gas contain carbon monoxide. The patient must have fresh air or oxygen inhalations In severe injury, venesection (letting of 300-500 ml. of blood) followed by injection of physiologic saline solution, 600 to 1,000 ml., is beneficial Muscular infusion of physiologic salt solution may be helpful during succeeding hours

Chloral Hydrate. If the victim is seen immediately, the stomach is lavaged. After sleep has become established, stimulants are administered.

Chlorine Gas and Similar Gases From Fluorine and Bromine. The inhalation of the hot vapor of weak ammonia, or vapor from a solution of 48 grains of sodium hyposulfite containing 12 grains of sodium carbonate or a teaspoonful of sodium bicarbonate in 5 ounces of water is comforting treatment

Cocaine and Eucaine. The lethal dose is 16 grains. If the patient is seen immediately, gastric lavage is performed and 200 to 300 ml of tea or coffee is instilled into the stomach Atropine (1/100 grain) may be given subcutaneously, or amyl nitrite inhalations may be tried Artificial respiration may be necessary.

Picric Acid. Poisoning with picric acid is treated by gastric lavage and the free administration of water by mouth.

Picrotoxin In treatment for barbiturate poisoning, picrotoxin may be given in excessive doses or accidentally administered There is no known antidote. Convulsions may be partially controlled by administration of chloroform (chloroform administered in the manner of chloroform *à la reine*).

Potassium Chlorate. The lethal dose is 80 to 240 grains. The stomach is washed and if necessary oxygen inhalations and venesection (500 ml.) are administered. The administration of acids, lemonade or acetates is avoided.

Pyrethrum. This poison is present in rotenone, a pesticide. The stomach is thoroughly washed with warm water, and 300 ml. of black coffee is instilled into the stomach. Artificial respiration and oxygen therapy may be necessary

Quinine. Thorough gastric lavage is followed by the instillation of 300 ml. of black coffee into the stomach Large doses of charcoal may be given.

Salicylic Acid (Sodium Salicylate and Aspirin). The stomach is cleansed with water or with a 1:1,000 solution of permanganate of potassium. One hundred milliliters of 1 per cent solution of sodium chloride is given intravenously Alkalies are not given unless the carbon dioxide-combining power and the blood pH are known. Dire results may ensue if an alkali is administered during the early phase of the respiratory alkalosis Alkalies may be necessary during the later phase of acidosis. Sedatives are administered for the hyperpnea and excitability.

Santonin. Santonin is lethal in doses from 1½ to 5 grains. Poisoning is treated by gastric lavage followed by chloral hydrate, 5 grains, repeated for the colicky pains If collapse has taken place, artificial respiration is given

Silver and Silver Nitrate. The stomach is washed out thoroughly with a solution (10 to 20 gm to 1,000 ml) of salt, and 30 ml of castor oil is given.

Sodium Hypochlorite and Sodium Hyposulfite Gastric lavage is performed with generous amounts of warm water or a weak solution of vinegar.

Strychnine. The lethal dose varies but is less than 20 grains. Apomorphine (5 mg.) is administered subcutaneously Rectal instillation of 15 grains of chloral hydrate and chloroform inhalations are useful Morphine is not used if artificial respiration seems necessary Venesection with letting of 500 ml. of blood has seemed to be helpful if followed by saline infusions

Sulfonal. The lethal dose is 160 to 480 grains. If the patient is seen immediately, the drug is removed by gastric lavage Artificial respiration, stimulants, epinephrine, picrotoxin or metrazol may be needed as in barbituric acid poisoning.

Sulfur and Sulfides Often artificial respiration and oxygen therapy are necessary. Venesection of 500 ml of blood followed by muscular infusion of physiologic saline solution is a recognized procedure Some good may be obtained from the administration of a solution of colloidal iron intravenously.

Thallium Gastric lavage with sodium thiosulfite is performed and 30 ml. of 3 per cent solution of sodium thiosulfite is administered intravenously BAL may be used as it is used for poisoning with arsenic (see Arsenic, p. 1422).

Turpentine. Gastric lavage with generous amounts of warm water or weak sodium bicarbonate solution is performed. Saline cathartics are recommended.

Veratrum Viride Lugol's solution in 15 minim doses is administered, and the patient is kept lying down and comfortably warm Artificial respiration and oxygen therapy may be necessary

Zinc (Zinc Chloride, Zinc Sulfate). The lethal dose is 80 to 160 grains. Gastric lavage with solution of sodium carbonate or of sodium bicarbonate, if the carbonate is not immediately available, is followed by the instillation of 300 ml of strong tea into the stomach Milk is given by mouth.

Lead Salts. These are lead acetate, white lead, lead oxide and red lead. The acute poisoning is treated by gastric lavage followed by the instillation of weak solution of sodium sulfate (1 per cent solution) into the stomach. Eggs, milk (eggnog), and charcoal may be given Lead colics are treated by opiates, atropine, belladonna and warm enemas

Lye The stomach is lavaged with dilute vinegar or lemon juice. Cream may be given by mouth. If more than an hour has elapsed since ingestion of lye, lavage is avoided and only aspiration of secretions from pharynx performed. Oral administration of olive oil in small amounts is made frequently Opiates may be required to allay the pain.

Mecholyl Atropine sulfate should be administered in doses of 0.25 to 0.6 mg. intravenously ($\frac{1}{250}$ to $\frac{1}{100}$ grain). If asthmatic attack is precipitated, epinephrine in the usual doses as indicated is employed. If the patient is in shock, administration of plasma or whole blood may be beneficial

Mercury (Corrosive Sublimate, Bichloride of Mercury). The lethal dose of corrosive sublimate is 8 grains. The mouth and stomach are washed with a solution of sodium perborate An eggnog is instilled into the stomach Infusions of dextrose and sodium bicarbonate are helpful

Methyl Alcohol (Methanol, Wood Alcohol) The lethal dose is 3½ ounces. Immediate gastric lavage is effected Venesection, letting from 500 to 750 ml. of blood, may be helpful. The patient is kept warm. Oxygen inhalations and stimulants such as caffeine and strychnine may be helpful in the presence of profound intoxications

Morphine (Opium, Codeine and Dionin) The lethal dose for adults is about 7 grains by mouth, about 4 grains subcutaneously; for children, $\frac{1}{15}$ grain The stomach is washed with 1 1,000 solution of potassium permanganate followed by the instillation of 300 ml of black coffee. Stimulation is applied to arms and legs to keep the patient awake if possible Artificial respiration may be required. The administration of atropine sulfate ($\frac{1}{100}$ grain subcutaneously, repeated) may be beneficial Strychnine sulfate, $\frac{1}{40}$ grain, may be given

Naphthalene (Moth Balls) A generous gastric lavage with water is the immediate treatment Oils are to be avoided, since moth balls are soluble in oil

Nicotine In pure form nicotine is lethal in doses of ½ grain Thirty to 50 grains of snuff or 75 to 200 grains of tobacco are considered to be lethal doses The effects of nicotine may be somewhat combated by the administration of morphine, ¼ grain, and atropine, $\frac{1}{150}$ grain, subcutaneously.

Nitrates Gastric lavage and external stimulation are the preferable treatment.

Oxalic Acid (Acid Potassium Oxalate). The lethal dose is 40 to 112 grains The stomach is washed with a solution of calcium, chalk lime or magnesium oxide. Subcutaneously or intravenously, 30 to 60 grains of calcium chloride in a quart of physiologic saline solution is administered.

Phenolphthalein To confirm diagnosis, a pink color should develop in the lavaged material on the addition of alkali. Phenolphthalein is present in cathartics such as analaz, ex-lax, phenolax and in some chewing gums.

Phosgene. Treatment for phosgene poisoning is given intravenously with injections of 10 ml. of 5 per cent solution of calcium chloride. The inhalations of the vapor from sodium bicarbonate solution (0.25 per cent solution) are comforting Venesection and the administration of 100 ml. of a 5 per cent solution of dextrose may be helpful.

Phosphorus. The lethal dose is about $\frac{1}{16}$ to 1 grain. The stomach is cleansed with a 1:1,000 solution of potassium permanganate. A solution containing 15 grains of copper sulfate is instilled into the stomach. The administration of sodium bicarbonate and lime water by mouth is helpful Milk, egg yolk, a [illegible] are avoided. Phosphorus burns are painted with a 10 per cent solution of silve

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repeated dental trauma over a long period, but only one, finger biting and toe biting, can be called a bite.

Dog Bites and Cat Bites. Owing to the configuration of the teeth of carnivorous animals which are designed to puncture and tear flesh, the bite of the dog, cat or any other carnivorous animal will be characterized by puncture wounds where the tusks enter the flesh and by tears. Such wounds are always heavily infected.

These wounds when made prior to death show evidences of trauma and hemorrhage. If made after death, they show no evidence of hemorrhage. There is a clean removal of tissues with jagged, chewed edges Sometimes the skin of the dead may be torn away over a wider area than that where the flesh has been eaten. The gnawing of the body of the dead, either man or animals, by rats produces the characteristic excavations made by these animals on cheese, wood, or any other solid material. There is a clean rough-edged removal of tissue which contrasts sharply with the jagged-edge wounds inflicted by the carnivora.

Cat Scratches and Cat-Scratch Disease (Nonbacterial Regional Lymphadenitis). The disease apparently is widespread. It has been reported as having occurred in many cities of the United States and France According to Daniels and MacMurray the first reported cases were associated with cats. The disease may be due to cat bite, injury to the skin by beef bone, thorns, wood splinter, mosquito bite, and laceration while butchering pork. The disease is probably due to a virus of the psittacosis-lymphopathia venereum group of viruses.

The patient is not severely ill, although in the early stages the temperature may be elevated and occasionally may reach 104 F (40 C) Headache is common but chills are rare A rash, either macular or vesicular, appears early in the disease, lasting 2 days The leukocyte count is usually normal but may be slightly elevated Erythema nodosum has been described

On examination a cutaneous lesion is present in one half of those incapacitated by this disease. The lesion develops at the site of a scratch or other injury to the skin. It may consist of a slightly raised erythematous nodule or plaque surmounted by a vesicle, pustule, or scab which may simulate a furuncle. The cutaneous lesion usually appears within a few days of inoculation However, it may not develop until after the regional adenopathy appears

Regional adenopathy may appear in 4 days after the cutaneous lesion, or its appearance may be delayed for as long as a month One or more regional lymph nodes may become so enlarged as to be evident on simple inspection.

In the limbs adenopathy is unilateral, involving the epitrochlear and axillary regions or the femoral or the inguinal regions More than half of the patients have involvement of lymph nodes of the head and neck, and of the anterior cervical, the posterior cervical, the submaxillary, the submental, or, occasionally, the occipital lymph nodes The nodes may remain movable and nontender or may become tender and progress to suppuration

The diagnostic skin test originated by Hanger and Rose according to Daniels and MacMurray utilizes the principle of the original Frei test. Pus is diluted 1 part to 5 parts with isotonic sodium chloride solution and heated at 56 C for 1 hour on 2 successive days. The test is performed by injecting 0.1 ml of the material intradermally and the result is read in 48 hours, when the reaction is maximal. A positive reaction is comparable with the tuberculin reaction and consists of a raised indurated papule measuring 0 5 to 1 0 cm. in diameter, surrounded by an erythematous areola measuring 3 to 5 cm or more in diameter. Rarely, the injection of antigen activates the primary lesion and may be associated with a rise in temperature

Rats and Rat Bites. Rats harbor and transmit the infectious organisms responsible for some 20 diseases of man. Some are serious and some are not. The

20

INJURIES AND DISEASES DUE TO ANIMALS AND PLANTS

INJURIES AND DISEASES DUE TO BITES AND STINGS OF ANIMALS OR TO INGESTION OF FISH OR MUSSELS

The natural method of injury to an opponent varies somewhat in different animals In the lower forms of life the methods of inflicting injury often are analogous to those employed in obtaining food, as exemplified in parasitism. The free-living animals of the lower orders inflict injury by employment of the sucking or biting apparatus, again as in obtaining food Many species of animals, right on up to and including man, use their bite for inflicting wounds for their protection.

Certain insects are provided with stingers equipped with adjacent apparatus for the injection of venom The sting and the venom too are apparatus employed for the getting of food

Certain reptiles such as serpents are equipped with fangs which are employed in the injection of venom These animals inflict wounds by their teeth and inject venom in order to kill their opponents for food or for protection to themselves

It is thus evident that the wounds inflicted by an animal for protection are usually analogous to wounds inflicted in obtaining food.

Human Bites. There are two considerations pertaining to human bites. (1) infection and (2) the presence of crushed tissues The lesions include necrosis of soft tissue and, as is often the case if the bite has been placed on the hand, tenosynovitis, and infections of the thenar and palmar spaces and the dorsal subcutaneous subaponeurotic space are common. Osseous and articular involvement may be obvious or it may be revealed on roentgenologic examination. The constitutional reaction to the infection is manifested by chills, elevated temperature, headache, malaise and leukocytosis The possibility of a bite should be borne in mind in any injury to the hand, particularly in one in which there is a foul discharge, and endeavor should be made to elicit the true history. The treatment, in early stages, for injury from a human bite is the conversion of the anaerobic state to an aerobic state and the excision of devitalized tissue in which the fusiform bacillus and spirochete might readily grow in symbiosis

A human bite is infected but it rarely is the means of transferring infections, that is, syphilis or rabies

Dental Injury. A distinction is made between a bite and a dental injury, either a self-inflicted bite or a bite by another person Hitting any part of the body against another person's teeth and sustaining an injury should not be called a bite For instance, a wound of a knuckle incurred by striking an opponent is correctly called a human tooth wound. Likewise a dental injury may be incurred from pressure in the process of finger sucking, or in lip biting, a nervous habit in which the lips may be accidentally injured. The affected person cannot resist these habits. In the case of finger sucking, a child will not fall asleep unless with his index finger all the way in the mouth. The lesion thus produced is similar in appearance and consistency to the lesions due to the actual chewing of the skin. Both are calluses from

tortrix). This snake inhabits high dry ground in the vicinity of swamps or marshy glades in parts of the eastern and all of the southern United States. The copperhead attains a large size, is vicious, and very dangerous.

Coral Snakes. The coloration and the body conformation of coral snakes are similar to those of a variety of harmless snakes For the purpose of quick identification it should be remembered that in the coral snakes the black rings over the back are broad and are bordered by narrower yellow rings, whereas in the nonpoisonous snakes of similar appearance the yellow rings are the wider and are bordered by black. Thus the rule. poisonous, narrow yellow-broad black-narrow yellow; nonpoisonous, narrow black-broad yellow-narrow black, in relation to the borders of the wide body stripes The coral snake is gentle and sluggish when handled; hence it too often is considered harmless Even after this snake has bitten a human being the wound, or series of wounds, because the coral snake does not strike like the vipers but rather tends to chew, are insignificant in appearance and may be ignored until serious symptoms develop.

After bites of a very small coral snake there may be only mild symptoms which appear in 15 minutes to an hour after the injury, with only slight pain at the site of the bite or bites There are dullness, apathy and weakness. When the bite is by a larger snake, there is pain at the site of the bite, and soon there are vomiting, profuse salivation, paralysis of the tongue and larynx, and in fatal instances death results from respiratory paralysis In all, the pulse is rapid and weak The pupils are often widely dilated and insensitive to light

Rattlesnakes, Moccasins and Copperheads The vipers bite by striking A strike will be made when the snake is provoked in any quarters, but when a person is bitten while handling the snake, the consequences may not be so serious as when the bite is given under more favorable conditions for the snake.

The maximal effective strike is made when the viper is coiled. Thus poised, the snake can make a strike at a distance equal to two thirds of the length of its body The strike, under these conditions, is delivered with a great deal of force, that is, a small dog will be knocked off balance by the strike. Stoic human beings describe the impact as stunning, at the moment they do not realize that they have been bitten by a snake The impact is so strong it is thought to be a quick violent blow of some sort As soon as the patient realizes what has happened, intense anxiety ensues

Symptoms Immediately after the bite, there is an intense burning pain at the site of the wound, swelling and darkening discoloration of the skin quickly spread and within a few hours may involve the entire bitten limb. There are immediate nausea, vomiting, giddiness and faintness, and within a very short period after the bite it may be difficult or impossible for the victim to walk In from 1 to 3 hours prostration and coma may be present The body is covered with cold and clammy perspiration The temperature falls below normal, the pulse becomes imperceptible, and death may result from paralysis of the upper nerve centers, usually a respiratory failure, for, as stated, all venoms contain varying amounts of the neurotoxin. If the patient survives, there is fever, and the course of the fever depends on the supervening infection which is always present.

Usually the severe constitutional symptoms pass off slowly, and by the second day the sensorium has cleared, the pulse is stronger, and the sweating has ceased

By the end of the first day the hemotoxic properties of the venom are becoming fully manifested The injured extremity is ecchymotic in appearance and the ecchymosis extends proximally in the bitten limb and often is manifested over other parts of the body The bitten limb is greatly swollen and there may be a generalized edema, with the face more profoundly affected than other parts of the body Vesicles containing hemorrhagic material form in the skin near the bite The site of the bite with surrounding parts may slough away and gangrene may supervene.

Owing to the hemotoxic qualities of the venom, jaundice is an almost constant

serious diseases transmitted by rats are bubonic plague, typhus and rat-bite fever Richter reported that he had observed that over a four-year period almost 25 per cent of the people in a rather large area in an American city had been bitten by rats Most of the bites were unimportant clinically, but hospital treatment was sought by nearly 100 persons from this area. In about a tenth of those who received hospital treatment for rat bites, rat-bite fever developed Uncaptured rats bite man, alive or dead, because they are hungry and they will continue to chew on him unless frightened away The situation cited is presumably not any worse than that in most other cities, and on farms Rats need no longer be endured since the advent of rat poisons which cause internal hemorrhages

Venom, Snakes and Snake Bites. Venom. Venom, composed of modified proteins, is the poisonous substance of the bites of some animals In the snakes it is secreted by glands connected by ducts to the poison fangs. The glands are analogous to the parotid glands in mammals The venom is squeezed out into the hollow fangs by contraction of the temporal muscles.

Venoms obtained from snakes, spiders, scorpions and other sources have proved to be highly antigenic substances. Protection against the action of venom has been obtained by the injection of antitoxins prepared in animals. Professional snake charmers, apparently immune, may have been immunized by injection of a particular preparation of venom These performers, however, before their act often cause their serpents to strike some object a sufficient number of times to exhaust the supply of venom

All snake venom contains mixtures of neurotoxins and hemotoxins, and the venom of all poisonous snakes contains some of the neurotoxic element which affects the higher nerve centers Immediate death (within a day) from snake bite is caused by respiratory paralysis The venom of the coral snake (like that of the cobra) is nearly all neurotoxins It acts on the nervous system, causing respiratory paralysis if injected in sufficient amount The venom of the vipers acts mainly on the vascular system, destroying erythrocytes and weakening the walls of the smaller blood vessels

Venom is not poisonous if it gets in the mouth (of a person who is sucking the bite of a snake or a spider on himself or other victim), for it is immediately destroyed by digestive ferments

Snakes. In the United States of America there are two groups of poisonous snakes, namely, the coral snakes and the pit vipers.

The coral snakes (family Elapidae, species *Micrurus fulvius,* and the subspecies *Micrurus* of Florida, Tennessee, Mississippi to Mexico) inhabit an area along the seaboard from the North Carolina coast southward, and westward along the Gulf coast to the Rio Grande River. The subspecies *Micruroides euryxanthus* is found in southern Arkansas, and in New Mexico and Arizona The northern limit of distribution is about latitude 35 degrees N

Of the pit vipers (group Viperidae, family Crotalidae) the rattlesnakes (species *Crotalus horridus,* the timber rattler, *Crotalus adamanteus,* the diamondback rattler, and the genus *Sistrurus* or pigmy rattler, and their variations, totaling some 15 to 18 subspecies) are the most widely distributed

A second pit viper in the United States is the water moccasin (*Agkistrodon piscivorus*), which lives along streams in the South It is the largest of the vipers, attaining up to 6 feet in length, and the most poisonous because of its correspondingly large dose of venom Many persons, believing that the water moccasin will not bite while in the water, have received bites from this snake. While in the water it not only can and will bite, but it is ready to bite. When the snake is under the water, it cannot strike hard enough to embed the fangs, but strike it will even while submerged Often it will slide from the limb of a tree, an habitual resting place, into the stream, swim to the water's edge, and rest on the bottom with its head above the surface, and body resting on the bottom, in which position it is ready for the strike.

A third pit viper is the copperhead (species *Agkistrodon mokasen,* synonym *con-*

has been discovered, its head and much of its body have been beaten into a pulp, so that it is not recognizable, even if available for identification.

If there is a good full pulse 2 hours after the bite, treatment should be instituted for wound infection as well as for the bite of the viper. If the patient is suffering no ill effects 2 hours after the bite no antivenin should be given.

One of every 5 persons bitten by poisonous vipers dies. The prognosis depends largely on the size of the snake and thus on the dose of venom injected. The period of disability is often of months' duration, owing to anemia and infection.

Antivenin is often available. It should be given up to ten hours after the bite if symptoms of poisoning have followed the bite.

Treatment for Snake Bites. *Local measures* are instituted to delay passage of the venom from the fang wound to the vital organs. Since much of the poison may be held for several hours in the edematous region surrounding the bite and absorbed gradually through the lymphatics, it may be removed in part by suction before it can permeate the body.

1 Apply tourniquet continuously to the limb about 2 inches above the bite, tightening it until the pulse can be felt faintly Do not pull it tightly enough to arrest the arterial circulation but only enough to restrict the venous and lymphatic return When a tourniquet is tightly applied and then loosened at intervals (15 to 20 minutes) the patient may go into shock. Shock may occur under these circumstances from sudden release of dammed blood if the tourniquet has not been loosened at the time interval specified, or it may result from the sudden release of venom into the circulation. (It should be possible to force a finger between the skin and the tourniquet.) If the limb becomes numb and cold, the constricting band is too tight. As swelling advances, move the tourniquet farther up the bitten limb

2. Cleanse with iodine the site of the bite and also the sharp instrument to be used for the incisions. Make incisions (preferably puncture wounds) ¼ inch deep, at the point where the fangs entered the skin and as swelling advances along the limb, make additional incisions at the edges of the swollen areas. For the bite of timber rattlers or other large snakes, deeper cuts may be necessary In cutting, be careful not to sever a large blood vessel, or a tendon, and avoid injuring the covering of bone. Apply suction by mouth, cupping glass or breast pump to produce free bleeding from these cuts. Viper venom does not readily penetrate the intact mucous membranes The mouth and throat may be further protected from infection by rinsing and gargling with dilute solution of potassium permanganate Swallowed venom is destroyed by the digestive juices in the stomach

3. Continue suction at the original bite and at each incision for periods of 15 or 20 minutes during each hour In the intervals between suction periods at each site, cover the individual wounds with cloths saturated with a strong solution of table salt or epsom salt in water

ANTIVENIN. As soon as possible (best within 2 hours) after the bite, antivenin should be administered and the tourniquet removed Antivenin may be given by the layman if a physician cannot soon be reached Prompt injection of sufficient antivenin prevents death in most patients, relieves pain and other local and general symptoms, aborts the serious effects, and shortens convalescence It is never too late to administer antisnakebite serum, and lives have been saved by injection of large doses even when the victims were apparently dying The danger is in undertreatment. Directions for administration of the antivenin are contained in the package

Refrigeration in the Treatment of Venomous Bites. Local refrigeration obtained by means of packing in ice the part injured by the bite of a snake or a spider is an efficacious method of treating such an injury It will control the pain, reduce swelling, retard absorption and promote the serous flow after incision and during suction

The treatment of snake bites by local refrigeration need not prevent treatment by the conventional methods such as incision, suction and the venous tourniquet. However, in all instances, it would be well to employ local refrigeration as soon as

feature following the bite of a viper. The jaundice may be clinically detectable at the end of 24 hours, and in the days immediately following may become intense

DIAGNOSIS The vipers theoretically have distinctive and characteristic bite patterns (Fig. 20-1A), owing to the arrangement of teeth and fangs This bite pattern, if well sustained, may be distinguished from that of the nonpoisonous snakes (of the United States) by the points of entry of the two fangs accompanied by the injury inflicted by a single row of jaw teeth, whereas in the nonpoisonous snake there are no double-pointed fang punctures of the skin. There is only a series of injuries corresponding to the double row of jaw teeth (Fig. 20-1B).

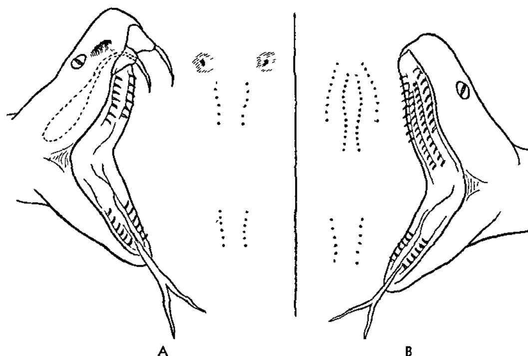


Fig 20-1. Mouth parts and types of wounds inflicted by them A, viper, poisonous snakes. B, nonpoisonous snakes

In practice these theoretic distinguishing features are often modified. The viper is rarely afforded a free range of movement in order that it may inflict a distinguishing wound. The strike is made obliquely on a moving object, for example a human limb, often one covered by clothing of uneven texture The cutaneous wound is a series of superficial scratches with one or two linear tears where the fang or fangs have entered Often one or both of the fangs are torn from the snake's mouth and left in the skin or the clothing

It is thus evident that immediately after the accident the differential diagnosis between the wound inflicted by a poisonous snake and that of a nonpoisonous snake is often difficult. In addition to these technical difficulties in differential diagnosis, man, and in fact all mammals, are inherently afraid of snakes The patient, if of nervous temperament, has abandoned all hope of survival and lies motionless, or may be difficult to keep quiet on account of fear. Commonly, as soon as the snake inflicts the bite, irrespective of whether the snake is poisonous, the skin and tissues about the wound are cut with a knife by the patient or by well-meaning friends Then the bites and the lacerations are sucked and often chewed by someone A tourniquet is applied, almost always too tight; as a result there are circulatory disturbances. In addition, the offending snake has usually crawled away, or if it

has been discovered, its head and much of its body have been beaten into a pulp, so that it is not recognizable, even if available for identification.

If there is a good full pulse 2 hours after the bite, treatment should be instituted for wound infection as well as for the bite of the viper. If the patient is suffering no ill effects 2 hours after the bite no antivenin should be given

One of every 5 persons bitten by poisonous vipers dies. The prognosis depends largely on the size of the snake and thus on the dose of venom injected. The period of disability is often of months' duration, owing to anemia and infection.

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ANTIVENIN As soon as possible (best within 2 hours) after the bite, antivenin should be administered and the tourniquet removed. Antivenin may be given by the layman if a physician cannot soon be reached Prompt injection of sufficient antivenin prevents death in most patients, relieves pain and other local and general symptoms, aborts the serious effects, and shortens convalescence It is never too late to administer antisnake-bite serum, and lives have been saved by injection of large doses even when the victims were apparently dying The danger is in undertreatment Directions for administration of the antivenin are contained in the package

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The treatment of snake bites by local refrigeration need not prevent treatment by the conventional methods such as incision, suction and the venous tourniquet. However, in all instances, it would be well to employ local refrigeration as soon as

possible, even though incision, suction and venous tourniquet has been employed before it was possible to use local refrigeration.

Ice packs have long been recognized as being helpful in the treatment of the bites of the black widow spider Frequently these bites are so situated that a venous tourniquet cannot be efficaciously applied

Gila Monsters. Gila monsters (species *Heloderma suspectum* and *Heloderma horridum*) are orange-and-black venomous lizards (beaded lizards) 10 or 12 inches in length or longer, which live in the deserts of Arizona and Mexico. Their poison-producing apparatus is situated in the lower mandible. The venom is secreted by the submaxillary glands, which are connected with grooved teeth. This animal bites while lying on its back.

The venom seems to contain considerable neurotoxin. Immediately there is sharp pain at the site of the bite, and there at once ensue weakness, nausea and vomiting There is weakness of the muscles and perhaps flaccid paralysis Dyspnea, venous congestion and cardiac dilatation with fast pulse are common symptoms In fatal bites death is from a respiratory paralysis

The diagnosis is usually obvious, for these sluggish animals are easily identifiable

Fish. Fish have frequently been implicated in *food poisoning*, particularly in tropical or subtropical areas However, it is evident from the following brief remarks that there seems to be much in common between this fish poisoning and staphylococcal food poisoning

In from 1 to 6 hours after eating the poisonous fish, the patient complains of a distinct metallic taste in the mouth and appears critically ill with severe gastrointestinal symptoms of nausea, vomiting, and diarrhea The skin becomes flushed and there are tingling and itching that may last for days Cramps in the extremities may occur Subsequently there may be weakness in the legs with possible temporary paralyses with reduced or absent knee jerks Hyperesthesias and paresthesias are commonly associated For instance, the patient interprets a cold object as feeling warm, or cold food as being hot, this effect in association with the metallic taste in the mouth is characteristic of fish poisoning There may also be associated nervousness, restlessness, or insomnia, albumin and casts in the urine and frequency of urination are prominent symptoms The illness may last from 1 to 3 weeks with gradual but certain recovery.

The symptoms differ from those reported following ingestion of certain Tetrodon fish found in Hawaiian and Japanese waters in which the active toxin, a leukomaine, has been isolated. In these instances the onset often appears within 15 minutes, and while gastrointestinal symptoms predominate there is a marked burning sensation The mortality rate is high. In lethal instances death occurs soon

Treatment for these poisonings is accomplished by immediate gastric lavage followed by the administration of castor oil (2 ounces).

There are a number of *salt-water fishes* which may injure sea bathers and novice fishermen by their *bites, stings*, or *body secretions* The eels of the genus *Muraena*, family Muraenidae, have specialized teeth associated with venom-secreting glands The venom is delivered onto the wound The various ray fish or sting rays, the Trygonidae, can inflict wounds The sting ray has a tail armed on the dorsal side with a barbed spine which in some species is capable of inflicting a poisonous wound Some ray fish, if stepped on in the water, may inflict a wound and contaminate it with tetanus The electric sting ray, family Torpedinidae, has a positively charged dorsal surface and a negatively charged ventral surface, and if an arm or a leg of a human swimmer makes contact with these two surfaces, it is temporarily paralyzed *Trachinus draco*, which resembles a trout, has a grooved spine passing through each gill which is equipped with a poison-secreting gland

Scorpaena scropha, a red fish with a large head and prominent fins, has a poison-producing gland connected with the first three rays of the dorsal fin. A person striking one of these fins experiences sharp pains at the point of contact. Soon a sensation of suffocation follows, delirium develops quickly, and death may ensue. First the area of skin about the wound is reddened, then it turns black and becomes gangrenous. These injuries should be treated with the same measures employed for snake bites except for the use of antivenin

In the United States the *fresh-water catfish* such as *Ameiurus* has a lancelike spine near the gills which may penetrate the hand while the fisherman is removing the fish from the crevices in rocks in which it has sought refuge from the noise and the muddying of the water resulting from the hunt. The small penetrating wounds from the lancelike spine are exceedingly painful and may be followed by severe systemic reactions and bad local infection.

Shellfish. Outbreaks of *mussel* or *clam poisoning* have occurred from Juneau, Alaska, to Southern California and the Gulf of California, Mexico

Shellfish poisoning, mytilotoxism, has been reported in certain shellfish in Nova Scotia. In a survey of commercially important shellfish areas of this region it has been found that paralytic shellfish poisoning is due to the shellfish from the Bay of Fundy only, off the coast of New Brunswick (Sommer and Meyer).

The poisoning is obtained from consuming shellfish or mussels which feed on the dinoflagellate *Gonyaulax catenella* The poison has not been identified, but it has been isolated and proved to belong to the class of alkaloids resembling strychnine, muscarine and aconite The poison has been isolated by chromatographic fractionation. It has been crystallized as rufinanate, helianthate and reineckate The purest preparation of mussel poison has a toxicity of 4 mouse units per microgram The concentration of mussel poison is expressed in mouse units of the poison contained in 100 gm of clam or mussel meat

This poison is one of the strongest known It is an alkaloid and is contained in plankton (*Gonyaulax*), comprising animal and plant life, a food for mussels In many parts of the southern United States it is traditional that fresh water mussels are poisonous, and consequently they are not eaten No specific treatment has been found for this disease.

About 15 minutes after poisonous mussels are eaten, there is nausea but not vomiting, and a feeling of drowsiness may ensue From 1 to 24 hours after ingestion of the mussels a general numbness around the lips, chin and cheeks and in the extremities is felt There is often a complete loss of power of the muscles of the extremities and neck A respiratory paralysis may ensue. Usually the numbness gradually disappears after 24 hours

Jelly Fish. Jelly fish (Medusae, genus *Obelia*) poison by ejecting barbs which cause a numbing effect and swelling and redness of the skin Occasionally there are urticaria and shock from this poison

Corals. Corals are formed by Coelenterata and Zoantharia (genus *Actiniaria*). When contact is made on abrasions, immediately there occur small blisters which itch, and irritation around the blisters is evident The whole area of skin affected becomes edematous

THE BITES AND STINGS OF INSECTS

Centipedes. The small centipedes (class Myriapoda) of temperate climates are often incapable of penetrating the skin, and their bites seldom produce more than mild, local symptoms In the southern United States two species, *Scolopendra heros* and *Scolopendra morsitans*, 10 to 15 cm in length, inflict painful bites. The larger tropical species, such as *Scolopendra gigantea*, 25 to 30 cm. in length, in addition to causing necrotic local lesions, may produce general symptoms of lymphangitis, fever, vomiting and headache.

Beetles. Beetles are facultative or incidental parasites of man. Canthariasis of the digestive tract, urinary system, nasal passages and sinuses, and skin occasionally occurs. This relatively rare condition results from the accidental ingestion of eggs, larvae, or adult beetles, or from their entrance into wounds or orifices of the body.

Blister or Vesicant Beetles. Blister beetles (order Coleoptera, family Meloidae) produce cantharidin, a toxic, volatile, vesicating substance. The commercial preparation, obtained from the Spanish fly, *Lytta vesicatoria* (*Cantharis* (*Meloe*) *vesicatoria*), and species of the genus *Mylarbris*, is used as a rubefacient, diuretic and aphrodisiac (U S Pharmacopoeia), although its internal administration is somewhat dangerous The *Lytta vesicatoria* is a southern European beetle which is abundant, particularly in Spain, in early summer

Vesicating lesions of the skin are produced by a toxic substance, perhaps different from cantharidin, which comes from rove beetles of the family Staphylinidae and from the commonly known blister beetles also Blister beetles are of medium or large size. The body is comparatively soft, the head is broad, vertical, and sharply narrowed into a neck, the prothorax is narrower than the wing covers, which are soft and flexible, the legs are long and slender, the hind tarsi are four-jointed, and the fore and middle tarsi are five-jointed Herms stated that they are named blister beetles because of their vesicating properties, that is, the application of the pulverized bodies or even the simple contact of many species produces a blistering of the skin.

More than 200 species of blister beetles have been found in the southern and western parts of the United States A common species in the East, of the genus *Epicauta*, colored a glossy deep purple, feeds principally on potato leaves and goldenrod pollen. Another common species is of the genus *Macrabasis* This is a black beetle, densely clothed with grayish hairs The Pennsylvania blister beetle, *Epicauta pennsylvanica*, also is a common species in the East.

The bites are received while the victim is visiting the woods or fields. Twelve to 24 hours afterward huge bullae occur, usually on the legs and neck, which heal in about 10 days. Rarely does the stranger to the community remember having been molested by the bug The bullae produced by vesicant beetles tend to be at the same stage of development about a day after contact with the insect. Characteristically, erythema is not present around the fully developed bullous lesion.

Differential diagnosis includes the cutaneous eruptions ordinarily characterized by bullae, that is, pemphigus, dermatitis herpetiformis, erythema multiforme bullosum, dermatitis venenata and bullae produced by thermal and chemical agents.

Honeybees, Wasps, Hornets, Yellow Jackets and Ants. Bees, wasps, hornets, yellow jackets, sawflies and some of the ants (order Hymenoptera) have ovipositors which are adapted for chewing, licking, and sucking plants. In some of these the mouth parts may be used to inflict injury to the human skin

Those possessing ovipositors adapted for stinging inflict injury to the skin by piercing it with the stinger and secondarily injuring it by the injection of venom. The stinger has a barbed sheath, a pair of serrated lancets, and a pair of lateral palps. The venom, secreted by glands, is forced down the canal formed by the sheath and lancets of the stinger. The exact nature of the active principle of this venom is unknown. It is a nonspecific poison of moderate toxicity During the act of stinging, the ovipositor is cast off by the honeybee and some wasps, but is retained by other species

All of these stings cause pain, edema and local inflammation Ordinarily the symptoms disappear after a few hours As in the poisonous snakes, the degree of severity of symptoms from the sting depends on the size of the dose of venom. The larger the insect, the larger will be the possible dose of venom. Likewise the amount of the inflammation depends on the location and number of the stings

In human beings the reaction to bee and wasp stings varies with the idiosyncrasy of the victims. The hardened bee keeper may be stung by 20 bees and have nothing to show for it but a few small, painless and transient pimples, while another person may be stung but once and die in a minute or two if he chances to be hyper-

sensitive to the venom. Hypersensitivity in human beings may take two forms: allergy and anaphylaxis. In the postmortem examination of persons killed by bee stings there are voluminous, overfilled, downy and emphysematous lungs, possibly exuding frothy fluid, overdistention of the right side of the heart and splanchnic dilatation and hepatic engorgement. The poison or antigen of bee venom is believed to reside in its protein.

The stinging ants of the temperate zones cause little injury, but the large, tropical species give rise to considerable pain and local inflammation and, if stings are numerous, may even endanger life.

Bee stings and ant bites are treated by the same therapeutic measures. Oral administration in usual therapeutic doses of an antihistaminic agent is indicated. Immediate application of an ointment with some massage alleviates pain and local swelling

Butterflies, Moths and Caterpillars. Butterflies, moths and caterpillars (order Lepidoptera) undergo complete metamorphosis The caterpillars are usually the voracious destroyers of plants and are the ones that injure the human skin

The severity of the dermatitis varies with the species of caterpillar, the site and extent of the exposure, and the sensitiveness of the victim. The lesions may be local or diffuse, according to the type of exposure Within a few minutes to several hours the exposed skin shows a vesicular erythema accompanied by an early burning or prickling sensation with numbness and pronounced itching. There are necrosis of the epidermal cells around the nettling hairs, the formation of vesicles, and inflammatory changes about the vessels of the corium In sensitive persons edema, urticaria and systemic symptoms may occur Windblown hairs may produce a severe irritative ophthalmia or serious inflammation of the respiratory tract

Grasshoppers, Locusts, Crickets and Cockroaches. The grasshoppers, locusts, and crickets (order Orthoptera) are seldom associated with diseases of man. The cockroaches, of the same order, have long been suspected of being mechanical carriers of certain human diseases.

The cockroaches (genus *Blatta*) are flattened, brownish, swift-running, omnivorous insects with legs of approximately equal length Of the five species which have become domesticated and generally distributed as common household pests, three species are most commonly encountered the oriental cockroach, *Blatta orientalis*, the German cockroach, *Blatta germanica*, and the American cockroach, *Periplaneta americana* The species are distinguished by variations in size and coloration. All cockroaches are of filthy habits, feeding on human excreta as well as on nearly all food consumed by man, and they invade kitchens and rooms where food is stored

Recently evidence of the cockroach as the agency in transmission of disease has been obtained Syverton and Fischer fed cockroaches with poliencephalomyelitis virus and collected fecal specimens daily. They found that for each of the first 6 consecutive days after the experimental feeding, the fecal suspensions contained sufficient virus, when injected into normal mice, to paralyze and kill mice in 2 to 4 days

Flies. Flies (order Diptera) from a medical standpoint are the most important of the orders of arthropods There are many species of bloodsucking and nonbloodsucking flies, some of which are intermediate hosts of animal parasites, and others, mechanical vectors of bacterial, viral and parasitic diseases

Bloodsucking Flies of the Families Muscidae and Hippoboscidae The bloodsucking stable fly (*Stomoxys calcitrans*), also known as the storm fly or stinging fly, is vicious in its attack just before storms or in late afternoon These flies cease attacking just before the sun goes down In the southern United States they are present the year round and are extremely abundant in some years. In the northern United States they appear only during the late summer and fall.

These flies bite by driving the distal half of the proboscis vertically into the skin. The proboscis is driven through the skin by three forceful depressions of the head,

as evidenced by the three sharp successive pains. After the extraction of blood there is discomfort for several minutes. A small roseola with a scarlet center persists for a long time. Almost always a few drops of blood trickle from the wound after the insect has fed.

Their habit of leaving one animal to resume feeding upon another makes stable flies ideal mechanical carriers of disease-producing agents, but so far the case is not proved against them

Tsetse Flies. The tsetse flies (species *Glossina palpalis* and *Glossina morsitans*) are almost entirely confined to equatorial Africa.

Glossina palpalis and allied species frequent the neighborhood of water and dense undergrowth. Their favorite localities are hot, damp areas on the borders of rivers or lakes Species of the *Glossina morsitans* group are less dependent on water than are the *Glossina palpalis* and are found in wooded and brush country that provides moderate shade. Tsetse flies bite more frequently toward evening after the heat of the day is passed than earlier

The bite of the tsetse fly is of minor consequence save as it serves to transmit African sleeping sickness to man and to animals.

Nonbloodsucking Flies. The nonbloodsucking flies affect the health of man by the mechanical transmission of disease-producing organisms and by the parasitic activities of their larvae.

The domestic species, usually of the families Calliphoridae, Muscidae and Anthomydidae, are the most important mechanical vectors Pathogenic bacteria, protozoa and helminthic ova are carried on the external structures (hairs, feet, legs and mouth parts) and in the intestinal tract of flies.

Maggots (Myiasis). Myiasis is the term applied to the invasion of living tissues of man by the larvae of flies, usually of the families Oestridae, Calliphoridae and Sarcophagidae.

Myiasis-producing flies may deposit eggs or larvae in or near living tissues, where the larvae inevitably become parasites This group may be subdivided into (1) flies that deposit their larvae in the habitat of the host, (2) those that lay their eggs or larvae on the hairs or body of the host, whence the larvae invade the local tissues and external atria or migrate to selective tissues, and (3) those that deposit their eggs or larvae in wounds and diseased tissue, where the larvae cause cutaneous atrial and wound myiasis without penetrating unbroken skin

Other myiasis-producing flies deposit their eggs or larvae in decaying flesh about wounds and thus may cause extensive destruction of tissue

Intestinal myiasis in man has been described, but this condition is largely accidental although some 30 species of dipterous larvae have been found in the digestive tract The intestine, however, is the normal environment of the parasitic gasterophilus larvae The accidental invaders, all flies that breed on decaying organic matter, are *Fannia canicularis,* the lesser house fly, *Eristalis tenax,* the rat-tailed maggot; *Aphiochaeta ferruginea* and *Aphiochaeta scalaris* of the family Phoridae; *Hermitia illucens,* the soldier fly, and *Piophila casei,* the cheese skipper. In infants the larvae of the flesh flies of the genus *Sarcophaga* may gain entrance through the anus when the eggs are deposited at the anal orifice. Many larvae are destroyed by the digestive juices, but others may be able to live in the intestinal tract and may produce intestinal distress.

The identity of the parasite causing a particular myiasis may be determined by rearing the adult fly from the larva, except in obligatory parasites that cannot be separated from the host.

Gnats (Eye Flies). The eye flies (family Oscinidae) are small acalyptrate flies about 2 mm. in length Those species that attack man and other mammals use the tips of the pseudotracheal rings of the labella as incising instruments for cutting the skin and conjunctival epithelium. Besides the initial injury a pathway for secondary infection is thus prepared.

The eye gnat (*Hippelates pusio*) spreads an acute seasonal conjunctivitis prevalent among children during the summer in California, and in Georgia and other southern states. Also the eye fly of India (*Siphunculina funicola*) and other species that feed on sores, wounds and conjunctival exudates are believed to be responsible for transmitting certain forms of ophthalmia

Botflies. The nonbloodsucking flies of the family Oestridae are known as botflies, warble flies or breeze flies.

In southern United States the larvae of botflies (genus *Gasterophilus*) affect man by getting into the cutaneous and subcutaneous tissues, causing slight pain, and their migrations produce creeping eruptions.

The larvae of botflies (genus *Oestrus*) may cause painful ocular and nasal myiasis in man.

Botflies (genus *Hypoderma*) affect the subcutaneous tissues and eyes of workers in animal husbandry. The lesion is furunculous in type. The larva may be removed by incising the furunculous lesion.

Blowflies Some of the species of these oviparous flies (family Calliphoridae), attracted by blood or offensive discharges, lay their eggs in cutaneous sores and abrasions, thus causing a myiasis with bloody irritating discharges from the wound

Tabanid Flies The Tabanidae have many common names horseflies, deer flies, mangrove flies, breeze flies, greenheaded flies, clegs and seroots. The family, most numerous of the Diptera, comprises some 60 genera and nearly 2,500 species. The important species are cosmopolitan but many have a local distribution The only species associated with the transmission of disease in man belongs to the genus *Chrysops*

The adult flies frequent stagnant water, hovering near the surface during the day Chrysops attacks man most actively from sunrise to 10:00 A.M. and from 4:00 P.M to dusk.

The bite of *Chrysops* is not immediately painful, although the act of withdrawing the mouth parts is usually noticeable, but within a few hours there is considerable local irritation and often extensive swelling, which may persist for days The flies usually attack the ankle, back of leg and outer side of hand. Tabanid flies are of medical importance, not only because they are biting pests, but also because certain species transmit diseases to man and animals. As mechanical vectors they may carry pathogenic organisms on their mouth parts and bodies *Chrysops discalis*, the western deer fly, as shown by Francis and Mayne is a mechanical vector of *Pasteurella tularensis* in man. Members of the other three common genera serve as mechanical vectors of anthrax and trypanosomal infections of animals

Screw Worm Flies Screw worm flies (genus *Chrysomyia*) similar in appearance and habits to *Cochliomyia*, are confined to Africa, islands of the Pacific, Australia and parts of Asia. These flies deposit eggs in or near wounds or external atria of mammals, and the larvae hatch within 10 hours The larvae produce foul-smelling, secondarily infected, mucopurulent lesions that may erode bone

The screw worm flies (genus *Cochliomyia, Cochliomyia americana, Cochliomyia hominovorax*, less common than *Cochliomyia macellaria*) are found in southern and southwestern United States and in greater numbers in tropical America. The eggs are deposited in small batches on the intact skin when the flies are attracted by purulent discharges and suppurating wounds. The larvae hatch in a few hours, penetrate the skin, and produce deep festering wounds. They can penetrate healthy tissues, even cartilage The turbinates and nasal septum may be destroyed, the sinuses infested and even the brain invaded through the middle ear. The fatality rate in man is about 8 per cent.

Flesh Flies The larvae of flesh flies (Sarcophagidae, genus *Wohlfahrtia*) cause extensive superficial furunculous lesions of the cheeks, neck, arms and chest of infants. These infections usually occur in June in infants sleeping unscreened out of doors.

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Several species of *Culicoides* are intermediate hosts of filarial parasites.

The bite of the midge produces an itching, rose-colored papule surrounded by an erythematous area 1 to 2 cm. in diameter. In sensitive persons the local lesions are pronounced and may be accompanied by nausea, fever and malaise.

Pappataci fever, sometimes known as sand-fly or three-day fever, is transmitted by members of the genus *Phlebotomus: Phlebotomus papatasii* and probably by *Phlebotomus perniciosus* and *Phlebotomus minutus*, all of the family Psychodidae and similar to the midges of genus *Culicoides*. This viral disease, most prevalent in the Mediterranean countries and southern Asia, resembles dengue

The exact role of *Phlebotomus* in the transmission of oriental sore and kala-azar is uncertain There is some evidence that Oroya fever, in South America, may be transmitted by *Phlebotomus verrucarum* and *Phlebotomus noguchi*.

The Simuliidae are called blackflies, buffalo gnats, turkey gnats and Kolumbatz flies. Like members of the families Culicoides and Psychodidae, they are important in the transmission of many diseases.

These small flies abound in the vicinity of clear, wooded streams. They shun bright sunlight and do not readily venture into the open Although they do not enter houses, they attack man on shady porches or in the vicinity of dwellings. They are a pest to fishermen and woodsmen and may incapacitate both men and animals

The bite, at first painless, except for a slight prickling sensation, later produces an ulcer-like sore due to the salivary toxin In susceptible persons there may be marked inflammation, local swelling and general incapacity. The flies most frequently attack exposed portions of the body, but they have the habit also of crawling beneath the clothing to inflict bites

Simulium damnosum and possibly *Simulium neavei* are the intermediate hosts of the filarial worm, *Onchocerca volvulus*, in Africa, and *Simulium metallicum*, *Simulium ochraceum* and *Simulium callidum* are involved in the transmission of Central American onchocerciasis *Simulium decorum katmai* is reported to be a vector of tularemia.

Lice. The order Anoplura (lice) includes two suborders: (1) Mallophaga (biting lice) and (2) Siphunculata (sucking lice). The suborder Siphunculata comprises four families, of which the family Pediculidae are important parasites of man.

The parasitic lice of man are (1) *Pediculus capitis* (head louse), (2) *Pediculus corporis* (body louse) and (3) *Phthirus pubis* (crab louse). The term Pediculus humanus includes both the head and the body lice. *Phthirus pubis*, the crab louse, is morphologically a distinct species. The head lice and body lice are apparently varieties of a single species. The body louse is believed to have been derived from the head louse, the result of a process of adaptation after man acquired the habit of wearing clothing Some authorities distinguish separate types of lice for the primary races of mankind, white, black, red and yellow. A distinctive species peculiar to African Negroes, *Pediculus maculatus*, has been reported

The body lice and head lice can move fairly rapidly and pass from host to host during contact The crab louse changes its position infrequently and moves only for a short distance It maintains a temporary position on the body of the host by clasping the hairs with its claws The favorite site for the head louse is the hairs of the back of the head, that of the crab louse the pubic hairs, and that of the body louse the fibers of clothing and the hairs of the chest and axillae

Lice suck blood for long periods but apparently never become engorged. During feeding the feces are dark red

During oviposition the female clasps a hair between the gonopods and the body so that the shaft is in contact with the genital opening. The eggs, called nits, are firmly attached to the hairs or, in the case of the body louse, to fibers of the clothing by a durable chitin-like cement. Eggs remain viable on clothing and blankets for a month

Characteristic cutaneous lesions are produced by the bites of both young and adult lice, the location varying with the three types.

House Flies. These flies (family Muscidae) include both bloodsucking and non bloodsucking species. Their geographic distribution is cosmopolitan.

The common house fly (*Musca domestica*) is the most abundant species of th Muscidae. House flies may cause an occasional intestinal myiasis; otherwise th common fly does no direct damage. It menaces health, however, as a mechanica carrier of pathogenic bacteria, protozoa and helminthic ova or larvae, chiefly thos of enteric diseases

Stable Flies. The nonbiting stable fly (*Muscina stabulans*) resembles *Musca domestica.* It is most persistent in its habit of trying to light about the mouth and nose of man, horse or cow Its larvae have been found in the human intestinal tract

Mosquitoes. The mosquitoes belong to the suborder Orthorrhapha, the family Culicidae The subfamily Culicinae is divided into three tribes: (1) Anophelini, (2) Culicini and (3) Megarhinini, of which the first two are of medical importance.

The identification of a species of mosquito requires training and experience.

The effect of the bite varies with the species of mosquito and with the susceptibility of the victim, some bites causing mild itching discomfort of short duration while others cause extreme irritation. Occasional persons manifest severe local symptoms of an allergic nature. The ordinary bite is followed by the appearance of wheals with erythema, swelling and itching lasting from a few hours to several days Vesicular bullae may appear and secondary infection may supervene.

The irritation is commonly but probably incorrectly believed to result from the salivary secretions injected into the wound. Numerous mosquito bites and poor personal hygiene may result in a severe dermatitis with fever and increased leukocyte counts

Mosquitoes as Vectors of Disease. Mosquitoes are the intermediate hosts in the transmission of four diseases of man: malaria, yellow fever, dengue and filariasis. Malaria and yellow fever have decimated and invalided large parts of total populations by becoming rampant because of the lack of protection from mosquitoes and a proper knowledge of their habits

Malaria Anopheline mosquitoes are the intermediate hosts of the plasmodia of human and simian malaria Of the 150 or more recognized species of anopheline mosquitoes some 70 have been incriminated as potential carriers, of which 19 are of major and 24 of minor importance. The remaining species are not natural carriers of malaria

Yellow Fever *Aedes aegypti* is the mosquito that transmits the virus of yellow fever. The mosquito can be infected only by biting the patient during the first 3 days of the disease; the virus requires an incubation period of 12 days before the mosquito becomes infective; and the mosquito remains infective all its life The rural and jungle types of yellow fever occur in Brazil, Colombia and Bolivia without the presence of *Aedes aegypti.* The existence of these types, with a possible animal reservoir, renders the complete elimination of yellow fever improbable.

Dengue. Dengue fever virus is transmitted chiefly by *Aedes aegypti*, but *Anopheles albopictus* and *Armigeres perturbans* have also been found to be vectors Infection is acquired by the mosquito during the first 3 days of the patient's illness

Filariasis. Mosquitoes are the vectors of two filarial parasites of man: *Wuchereria bancrofti* and *Wuchereria malayi*

Culex fatigans, a night-biting mosquito, transmits *Wuchereria bancrofti. Aedes variegatus,* a day-biting mosquito, also is an important host in the Pacific islands. Complete development has been recorded in 22 species of *Anopheles.*

The principal carriers of *Wuchereria malayi* belong to the genus *Mansonia*

Midges, Sand Flies and Gnats. The midges (genus *Culicoides*) live and swarm [illegible] they bite most actively at dusk or [illegible] ammals. The midges of [illegible] a are nocturnal feeders. [illegible] ht of midges. Their small

size enables them to pass through 16-mesh screening.

Ctenopsyllus segnis, the mouse flea, is a common parasite of the house mouse, rat and other small rodents.

Tunga penetrans, the chigoe, chigo, nigua, jigger or sand flea (sometimes erroneously called chigger), is a parasite of man, hogs and dogs in tropical America and Africa Man is infected by contact with soil infested with immature fleas The site of infection is usually the feet and sometimes the hands

The female jigger, *Tunga penetrans*, after fertilization burrows into the skin, usually about the toes, soles of the feet, fingernails or interdigital spaces, and after engorging herself with blood becomes distended with eggs

The lesion, at first characterized by a central black spot in a tense pale area, becomes a festering sore Secondary bacterial infection may produce an extensive dermatosis and a painful ulcer

Diagnosis is suggested by the bites and confirmed by finding the fleas and identifying them

Fleas as Vectors of Disease Fleas transmit plague, endemic typhus and cestode infections.

Plague. The bubonic and septicemic types of plague, due to *Pasteurella pestis*, are transmitted from rat to rat and thence to man by fleas Epidemics of plague among these wild rodents give rise to infection in rats The spread of the disease in man is chiefly due to the rats associated with human habitations, such as the brown rat (*Mus* (*Rattus*) *norvegicus*) and the black rat (*Mus* (*Rattus*) *rattus*) On the death of the rat the infected fleas seek new hosts, either man or other rats

The most dangerous fleas are those susceptible to infection and to bacterial obstruction of the proventriculus, but the feces of all diseased fleas are infectious.

Typhus Fever Endemic typhus fever, a mild form of *Rickettsia prowazeki* infection occurring sporadically in the United States of America, is transmitted by fleas from rat to rat and from rat to man The common insect vectors are *Ceratophyllus fasciatus* and *Xenopsylla cheopis*. The organism of murine typhus may remain viable for at least 651 days in the infected feces of the flea. Infection occurs by contamination rather than by the bite of the flea

Cestode Infections The rat fleas, *Ceratophyllus fasciatus*, *Ceratophyllus wickhami* and *Xenopsylla cheopis*, the mouse flea, *Ctenopsyllus segnis*, the dog flea, *Ctenocephalides canis*, and the flea of humans, *Pulex irritans*, are hosts of *Hymenolepis diminuta*.

True Bugs (Order Hemiptera) *Bedbugs* The common bedbug, *Cimex lectularius*, and the oriental bedbug, *Cimex hemipterus*, family Cimicidae, are parasites of man. They flourish in warm climates and are more abundant in plains and valleys than in mountainous regions

Bedbugs are nocturnal in their habits, concealing themselves during the day in the crevices of bedsteads, in closets and cabinets, in wainscoting or under loose wallpaper. Both nymphs and adults feed at night on man and small mammals They survive starvation for more than a year, a fact which accounts for their presence in houses long unoccupied

The bite of the bedbug ordinarily produces red itching wheals and causes loss of sleep Some persons show no reaction, others have urticaria, and still others manifest allergic symptoms Asthma has been caused by *Cimex lectularius*.

The bedbug is not a proved vector of human diseases

Reduviid Bugs Species of *Triatoma* and *Rhodnius* (family Reduviidae) are called cone-nosed bugs because of the pointed head, barbers because these insects bite the face, assassin bugs, and flying bedbugs They are dark brown with red or yellow markings on the thorax, wings and sides of abdomen

Several species of reduviid bugs frequent houses They hide during the day in dark recesses and feed at night They move rapidly both in flight and on foot Only occasionally do they bite man and other mammals

The two genera most concerned with the transmission of human disease are *Triatoma* and *Rhodnius* *Reduvius personatus*, the widely distributed and notorious "kissing bug," attacks the face, particularly the lips, often causing intense pain Other species also inflict painful bites. *Triatoma sanguisuga*, the Texas or Mexican

The irritating saliva, injected during feeding, produces a roseate elevated papule accompanied by severe itching Persons with pale delicate skin react more violently than those who have dark skin Scratching increases the inflammation and leads to bacterial infection with the sequelae of pustules, crusts, suppurative processes and matted hair. Severe infestations may lead to scarring, induration and pigmentation of the skin and even ulceration. Infestation of the eyelashes through secondary infection leads to phlyctenular conjunctivitis and keratitis.

Itching is the earliest and most prominent symptom and with the crab louse is especially severe at night. The sequelae of scratching are the most characteristic signs. Old and debilitated persons are most severely affected. In these patients bacterial dermatosis is common; occasionally death may result from ensuing septicemia.

Peck, Wright and Gant have determined the component cutaneous injuries due to the bite of the louse. They have expressed the belief that repeated exposures of the skin to ravages of the body louse result in the development of a dermal hypersensitivity This dermal sensitivity is the result of the action of the feces on the skin. It seems that there are two components to the louse-bite reaction. (1) the purpuric element due to the act of feeding and (2) the development of an inflammatory reaction following skin sensitization The pruritus accompanying infestation with lice seems to be mainly a part of the syndrome of hypersensitivity.

The diagnosis of pediculosis depends on finding the adults or the nits

Lice as Vectors of Disease The body louse is the vector of typhus fever, trench fever, and European relapsing fever The head louse is a less important vector than the body louse, the crab louse has never been incriminated. Temperatures greater or less than the normal body heat of man are unfavorable for lice Lice will leave a febrile patient and seek other hosts, thus increasing the chance of spreading infection Lice crawl away from their dead host.

Typhus Fever Typhus fever, caused by *Rickettsia prowazeki*, is spread by infected lice. Lice become infected by ingesting the blood of a diseased person. Man acquires the infection through contamination from the feces or the crushed body of the infected louse, or when bitten by a contaminated proboscis. The louse remains infective throughout its life

Trench Fever Trench fever is caused by *Rickettsia quintana* The louse becomes infected by the ingestion of the blood of a person sick with trench fever. Infection of a new host occurs as in typhus fever.

Relapsing Fever The European form of relapsing fever is caused by the spirochete *Borrelia recurrentis* The organisms are ingested with blood by the louse Man is infected by the contaminative method, the crushed body of the louse coming in contact with the bite or broken skin

Fleas. Fleas (Siphonaptera) are ectoparasites. Man is the principal host of *Pulex irritans*, an important host of *Tunga penetrans* and an incidental host of several species parasitic to other mammals.

The cutaneous irritation caused by the salivary secretions of fleas varies with different persons Some show no reaction while others have a raised, roseate, slightly edematous lesion at the site of the bite. There are still others who are susceptible who will have extensive inflammation manifested by papular rashes.

Pulex irritans, the flea of humans, is the flea most commonly found on man in houses in Europe and western United States

Echidnophaga gallinacea, the sticktight flea, or southern chicken flea, occasionally infects man. Its burrowing habits are similar to those of *Tunga penetrans*. It ranges in the southern United States of America as far north as Kansas.

Xenopsylla cheopis, the Indian rat flea, is the most important flea associated with the transmission of bubonic plague. It attacks man and other mammals as well as its natural host, the rat

Ctenocephalides canis is the commonest species found in house infections in eastern and southern United States.

The symptoms from the bite vary with the site of the injury and the amount of injected venom. The symptoms are both local and general The lesion is a minute, nonelevated bluish red spot with a white areola that speedily disappears, or it may become red and swollen Urticaria and vesiculation may appear about the site. The bite produces a sensation of lancing which is followed by a latent period of 10 or 15 minutes, at the end of which the generalized symptoms supervene. These symptoms follow a uniformly progressive course, corresponding to the stages of (1) lymphatic absorption, (2) vascular dissemination and (3) elimination of the toxin. Lymphatic absorption is evidenced by the proximal progress of throbbing, lanceolating pains and numbness in the affected part In from 15 minutes to several hours the evidences of the vascular dissemination ensue Agonizing muscular pains increasing in intensity spread over the abdomen. The local pain recurs and rapidly increases to involve the entire body. Clonic contractions, tremors, spasmodic movements and convulsions follow The symptoms and pains are intermittent and reach their maximal intensity in the waist, arms and legs. The muscular contractions and the excruciating pain bring about rigidity of the abdomen and of the chest. The patient experiences precordial and abdominal oppression and has the feeling of approaching death. There may be disorientation, hallucinations, delirium, debilitating sweats, profuse salivation and lacrimation. The sensitivity of the skin and the reflexes are exaggerated The respirations are rapid and shallow Temporary tachycardia is followed by bradycardia The arterial pressure increases and later falls. Albuminuria is always present and uremia may develop. Intestinal and vesical paralysis develop There may be priapism, ejaculations and enuresis After a few hours, the period of elimination of the toxin begins The symptoms abate somewhat, only to return in paroxysms. The disorder persists for a week.

The convalescence is characterized by physical and mental fatigue The bite confers a temporary immunity In animals the immunization persists for about 3 months. Persons have been bitten by *Latrodectus mactans* several times and each time have had all the symptoms of poisoning.

DIAGNOSIS It is often alleged that arachnidism is to be differentiated from acute, surgical conditions in the abdomen, particularly ruptured gastric or duodenal ulcers. It does not seem likely that such a state of diagnostic confusion should exist The history of the spider bite and the spreading course of the cramping muscular pains are not likely to be confused with anything else.

The mortality rate is 4 to 5 per cent Children are more susceptible than adults.

TREATMENT. Ten milliliters of calcium gluconate may be given intravenously. Hot tub baths give some relief *Latrodectus mactans* antivenin may be given intramuscularly, dose 2 5 ml, and may be repeated in 1 to 2 hours if symptoms are not relieved The site of bite is cleansed to prevent secondary infection.

Scorpions. Of the numerous species of scorpions (order Scorpionida) throughout the world, some 20 or more are found in the southern United States and many more in Mexico Some of the larger scorpions injurious to man are *Buthus quinquestriatus* of northern Africa and southern Europe, *Centruroides suffusus* and *Centruroides noxius* of Mexico, and *Centruroides sculturatus* of Arizona.

Scorpion venom is a clear, colorless toxalbumin containing a variety of toxic substances In mice it produces paralysis, nervous disturbances, convulsions and pulmonary disorders

[illegible] contact with [illegible] cause only [illegible] roduce serious and even fatal systemic reactions.

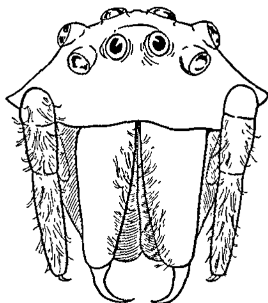
In man the local symptoms of scorpion poisoning are mild. A small, red spot at the site of the sting is followed by slight swelling and excruciating pain that last several hours and subside the following day. Nervous reactions are often severe,

bedbug, has a taste for human blood. It remains hidden during the day and is a nocturnal feeder. Its bite is severe and causes swelling accompanied by itching

Chagas' Disease. Probably all species of *Triatoma* and *Rhodnius*, and even those of *Eratyrus* and the several other related genera, are capable of transmitting *Trypanosoma cruzi*. The trypanosome, introduced into the intestinal tract of the bug during feeding, undergoes a cyclic development in the midgut and hindgut during a period of about 20 days. Infection is usually transmitted by the bug through fecal contamination of the bite, though occasionally directly through regurgitated blood The reduviid bug remains infective for years.

Spiders. The large hairy tarantulas of the family Aviculariidae inflict only slight or, at most, painful injury on man. The small black spiders (black widow), of the genus *Latrodectus*, family Theridiidae, however, possess a potent venom that produces serious symptoms in man. Spiders of this genus range from southern Canada to Chile In the United States of America these spiders are most abundant in the far western and southern parts. The female black widow spider is considered to be the only spider residing within the continental United States capable of inflicting serious injury to man

Black Widow Spider (*Latrodectus mactans*). Only the female is harmful, the male is too feeble to inflict injury. The black widow, so named because of her shining black body and her habit of devouring her mate after copulation, is known also as the hourglass, shoe-button or pokomoo spider.



Modified from Thorp and Woodson, Black Widow America's Most Poisonous Spider, Univ North Carolina Press, 1945

Fig 20-2. Mouth parts of the black widow spider (stripped of most of the hairy coverings)

The over-all length (legs extended) of the female is about 1½ inches (38 mm.), the length of the body about ½ inch (13 mm.), and the width of the abdomen about ¼ inch (6 mm.) The male is much smaller, from one third to one half the size of the female The thorax is brown or black, the long slender legs are dark brown or black, and the abdomen jet black. The legs and body are covered with short black hairs. The female has a variable, median, orange or red spot in the form of an hourglass or Maltese cross on the ventral surface of the glossy, globose abdomen, and almost always there are red markings on the dorsal surface of the abdomen The head and mouth parts are vicious in appearance when viewed clearly without most of their hairy coat (Fig 20-2).

The black widow bites only when disturbed; unfortunately she is easily disturbed. The spider infests piles of wood, wooden fence posts, stumps, undersides of privy seats, outbuildings, cracks in basements, and houses. A favored dwelling is at the junction of an out-of-doors clothesline and its post, from which vantage point the spider often bites women about the face and neck while they are hanging out the washed clothes This spider may get into beds and here may bite any part of the body, but seemingly the bites inflicted in bed are usually about the face and eyes The most frequent situation of bites, however, are the buttocks and the penis, which are bitten while the victim is using the privy.

Symptoms The black widow's nonhemolytic venom, probably a toxalbumin, affects the nerve endings. However, she may and can bite without injecting venom

morphic stages in the tick, and may be transmitted through the eggs to succeeding generations

Diseases transmitted by ticks to man comprise some such listing as the following (from Belding):

BACTERIAL AND SPIROCHETAL DISEASES

Tularemia. *Dermacentor andersoni*, *Dermacentor variabilis*, *Ixodes ricinus*, and *Ornithodorus turicata* and *Ornithodorus parkeri* (experimentally), the United States of America; species of *Ixodes*, Russia, *Hyalomma aegyptium* (experimentally) Greece.

Relapsing fever (for example, *Borrelia duttoni*). *Ornithodorus moubata*, southeastern Africa; *Ornithodorus erraticus*, northern Africa; *Ornithodorus marocanus*, Spain and Morocco; *Ornithodorus papillipes*, central and eastern Asia; *Ornithodorus savignyi*, eastern Asia; *Ornithodorus venezuelensis* and *Ornithodorus talaje*, South and Central America and Mexico, *Ornithodorus turicata*, Mexico and the United States of America, *Ornithodorus hermsi* and *Ornithodorus parkeri*, the United States of America, and *Rhipicephalus sanguineus*, Africa.

VIRAL DISEASES

Equine encephalitis (western strain). *Dermacentor andersoni* (experimentally), the United States of America.

Yellow fever· Experimentally *Ornithodorus moubata*, Africa, and *Ornithodorus rostratus* and *Amblyomma cajennense*, Brazil.

Spring and summer encephalitis *Ixodes persulcatus*, *Dermacentor silvarum* and *Haemaphysalis concinna*, Russia

Lymphocytic choriomeningitis *Dermacentor andersoni* (experimentally), the United States of America

Colorado tick fever *Dermacentor andersoni* (suspected), the United States of America.

RICKETTSIAL DISEASES

Rocky Mountain spotted fever (*Rickettsia rickettsi*) *Dermacentor andersoni*, *Dermacentor occidentalis*, *Dermacentor variabilis* (eastern type), and experimentally *Dermacentor marginatus* and *Amblyomma americanum*, the United States of America.

Boutonneuse fever *Rhipicephalus sanguineus*, Mediterranean countries.

African tick typhus *Rhipicephalus sanguineus*, *Rhipicephalus appendiculatus*, *Amblyomma hebraeum*, *Boophilus annulatus* var *decoloratus*, and *Hyalomma aegyptium* (experimentally).

Russian tropical typhus *Dermacentor nuttalli*

São Paulo fever (*Rickettsia braziliensis*) *Amblyomma cajennense*, *Amblyomma striatum* and *Rhipicephalus sanguineus*, Brazil

Montana "Q" fever (*Rickettsia diaporica*) *Dermacentor andersoni*, the United States of America

PROTOZOAL DISEASES

American trypanosomiasis (*Trypanosoma cruzi*) Experimentally *Amblyomma cajennense*, *Rhipicephalus sanguineus*, and *Ornithodorus moubata* and other species of *Ornithodorus*

This listing is regularly being added to as more care is taken in the identification of a tick found to be a vector of disease.

To remove the embedded head of a tick, apply a few drops of whisky, alcohol, ether, kerosene or white gasoline

Mites. Some mites (order Acarina other than the Ixodoidea or ticks) cause direct injury to man and others transmit human diseases

Red Bug. Red bugs (family Trombidiidae) are usually bright red but may be ornamented with red, orange or black spots The six-legged larvae are the bloodsucking parasites of animals

with throbbing and muscular twitching of the fingers, toes, ears, nose and chin accompanied by itching and paresthesia Other symptoms are headache, giddiness, nausea and vomiting, profuse perspiration, cold extremities, subnormal or slightly elevated temperature and feeble pulse. When the poison is fatal, respiration is accelerated and death results from pulmonary edema

In the south central part of the United States persons observed immediately after having been stung by large scorpions appear pale. They are nauseated and vomit. They complain of being too weak to walk. Examination of a person who has been effectively bitten or stung by a large scorpion below the knee reveals that the weakness complained of is actually a flaccid paralysis of the extremity This paralysis may involve the opposite leg to a slight degree. After 2 to 3 hours the paralysis passes and leaves no residua

Ticks. Ticks are divided into two large families, the Argasidae or soft ticks with two genera, and the Ixodidae or hard ticks with several genera. The argasid ticks are more primitive than the ixodid ticks, are less constantly parasitic, produce fewer progeny and infest the habitat of the host. The ixodid ticks are the more specialized and more highly parasitic, produce more progeny and infest the migratory host itself

Ticks injure man and lower animals in three ways: (1) by the irritation of their bites, (2) by producing tick paralysis through their poisonous secretions and (3) by serving as vectors of bacterial, rickettsial, viral and protozoan diseases.

The insertion of the capitulum into the skin produces an inflammatory reaction of the perivascular tissues of the corium with local hyperemia, edema, hemorrhage, and thickening of the stratum corneum. Occasionally ticks (*Ixodes ricinus*) burrow beneath the skin

A severe localized dermatosis often follows if a part or all of the tick's head is broken off and left in the skin

Tick Paralysis. Tick paralysis occurs in northwestern United States, southwestern Canada, South Africa, Australia and Crete. Sheep are commonly affected, cattle and dogs less frequently, and man and cats occasionally. The disease is usually associated with *Dermacentor andersoni* in North America, *Ixodes holocyclus* in Australia and *Ixodes pilosus* in South Africa, though other species, including *Ixodes ricinus, Rhipicephalus simus* and *Dermacentor variabilis,* have been implicated.

The probable cause of the paralysis is a toxic substance secreted by the salivary glands of the tick rather than a neurotropic virus, since the onset of symptoms, 9 to 16 days after attachment, corresponds to the time of engorgement, and the removal of the ticks permits recovery after paralysis has started The toxic substance is possibly elaborated by the ovaries.

SYMPTOMS. Children are usually affected, adults rarely except, occasionally, aged individuals. Age immunity apparently depends on the size of the host in relation to the amount of toxic secretion; children less than 2 years of age succumb rapidly. The intoxication is the most pronounced when the ticks are attached to the neck or along the spinal column

The disease is a progressive, ascending, flaccid motor paralysis The early symptoms are malaise, lack of appetite, irritability, in-co-ordination, and paralysis of the lower extremities, at times with loss of reflexes. There may be diarrhea, convulsions, and a slight fever or a subnormal temperature. The paralysis ascends to the muscles of the thorax, deglutition and speech, and also involves the involuntary muscles of the anal and vesical sphincters Most affected persons recover. When death results, it is due to respiratory paralysis.

Treatment of man involves the complete removal of ticks and their capitula by hand. As soon as the tick is removed, recovery ensues.

Ticks as Vectors of Disease. Ticks are recognized as vectors of disease in man. In many species of ticks the organisms of disease are carried through the meta-

other mammals. The *Sarcoptes scabiei* is cosmopolitan in distribution and lives solely in the skin of man.

The preferential sites of habitation are between the fingers and toes, the flexor surfaces of the forearm, shoulder blades, small of back, the inguinal region and the genitalia The lesions, minute, translucent, vesicular swellings, appear as slightly reddish elevated tracts on the surface of the skin The intense itching, aggravated by warmth and perspiration, causes scratching, which spreads the parasite, irritates the lesions, and induces secondary bacterial infection. As a result multiple papular, vesicular and pustular lesions may be produced. Unless treated, a chronic condition may ensue, and severe infestations may prove a serious health hazard.

The type and distribution of the lesions are characteristic Conclusive evidence of the infestation is obtained by removing the mite from its burrow with a needle.

Mites of Blackheads. Blackheads result from an obstruction to hair follicles. In some blackheads there is a mite (family, Demodicidae, and one genus, *Demodex*) which does not seem to cause any discomfort. Occasionally, however, when there are many mites present, a dry chronic erythema with burning irritation and scaling of the epidermis occurs.

DISEASES AND INJURIES DUE TO CONTACT WITH PLANTS AND INGESTION OF PLANTS AND PRODUCTS OF PLANTS

Plants Causing Cutaneous Injuries. The following list compiled by Muenscher in *Poisonous Plants of the United States* (1951), includes plants that have caused dermatitis The part of the plant that most frequently causes dermatitis on contact is indicated for each species. Many of the plants produce dermatitis only occasionally or in persons who are especially sensitive. Some species cause poisoning of many but not all persons who come in contact with them. In addition to these cases of dermatitis, many instances of occupational dermatitis result from the handling of certain plants or plant products in certain industries.

Ailanthus altissima—Tree-of-heaven	flowers, leaves
Anacardium occidentale—Cashew-nut	"husks" of nut
Anagallis arvensis—Scarlet pimpernel	leaves
Anthemis arvensis—Corn chamomile	leaves and flowers
Anthemis cotula—Dog fennel	leaves and flowers
Aralia spinosa—Hercules club	bark
Arctium lappa—Great burdock	leaves
Arisaema triphyllum—Jack-in-the-pulpit	leaves, corms
Asarum canadense—Wild ginger	leaves
Asimina triloba—Papaw	fruits
Asparagus officinalis—Asparagus	young stems
Borago officinalis—Borage	leaves
Buxus sempervirens—Box	leaves
Cannabis sativa—Hemp, marijuana	leaves, flowers
Catalpa speciosa—Catalpa	flowers
Caulophyllum thalictroides—Blue cohosh	rootstocks
Chelidonium majus—Celandine	juice
Chimaphila umbellata—Princes-pine	leaves and stem
Clematis virginiana—Virgins-bower	leaves
Colchicum autumnale—Autumn crocus	leaves
Conium maculatum—Poison-hemlock	leaves
Convallaria majalis—Lily-of-the-valley	leaves
Cypripedium reginae—Showy lady-slipper	hairy leaves and stems *
Cypripedium parviflorum—Yellow lady-slipper	hairy leaves and stems *
Daphne mezereum—Daphne	bark
Datura stramonium—Jimson-weed	leaves, flowers, fruits
Daucus carota—Wild carrot	leaves

* The most troublesome species.

Chiggers, the larvae of the North American red bug *Eutrombicula* (*Trombicula irritans*), commonly infest grasses and bushes, particularly wild vines, whence they attack animals and man. The adult red bug is a scaveng the feces of insects and decaying woody substances It is an orange-red m meters in size though 5 times larger than the larva, and lives for about 10 mo

The larvae attach themselves to the skin by the capitulum and after meal drop off in 3 to 5 days. They select the thin, tender, wrinkled surfaces, such as the popliteal region and waist, passing actively up th seldom going above the waist if a belt is worn. If there is no belt, the n the anterior part of the abdomen and chest and the axillae. Women ar are more susceptible than men Attachment takes place within a few mi exposure Itching begins within an hour or two and reaches a maximum part of the first 24 hours During the second day the swelling subsides a pinkish color, which gradually turns to a deep red by the third day, sur puncture point Vesicles frequently occur. The discoloration disappears seventh day. Severe infestations may produce fever. The patient suffe discomfort and torture with attendant loss of sleep. The mites may be re rubbed off or scratched off with the fingernail

The Japanese species (*Trombicula akamushi*) is a proved vector o mushi disease or Japanese river fever

Chicken Mite The chicken mite (*Dermanyssus gallinae*) attacks hum if they are around the infested habitations of chickens Its bite causes dermatitis, usually on the backs of the hands and forearms.

Rat Mite The rat mite (*Liponyssus bacoti*) is prevalent in the United States around stores, factories, warehouses and stockyards. Its bite a vesicular dermatitis with urticaria. Subsequent scratching may cause infection This mite serves as a vector for the transmission of endemic ty rat to rat The rickettsial organisms are passed from one generation to through the eggs of rat mites.

Grain Itch Mite. The grain itch mite (family Pediculoididae, a spec genus *Pediculoides*) produces dermatitis among workers in grain The m *culoides ventricosus*) feeds on the larvae of insects that infest wheat, b other grains and straw

Large numbers of these mites may spread over the entire surface of t of threshers, grain-handlers and persons sleeping on straw mattresses. burrow superficially in the skin, producing local petechiae and erythema fo wheals, vesicles and pustules They cause an annoying pruritus sometim panied by high fever, temperature of 103 or 104 F (39.4 or 40 C)

Itch and Mange Mites. Some of these mites (superfamily Tyrogly infest foods. Grocers' itch is caused by several different mites (genus *Gl domesticus*, of sugar; genus *Tyroglyphus Tyroglyphus siro* of cheese, *Ty longior*, of cheese and cereals, *Tyroglyphus farinae* of flour, grain and Coolie itch is caused by a mite (*Rhizoglyphus parasiticus*). Both the egg mites of the cheese mite are found in human feces, without any injury in t tive tract attributable to their presence

The itch and mange mites, except for the genus *Sarcoptes* and the g *toedres* (family Sarcoptidae of superfamily Sarcoptoidea), are nonburrowi they produce irritation resulting in many-layered scabs on the skin.

Scabies (Seven-Year Itch). The mites of scabies belong to the genus *Sar* the superfamily Sarcoptoidea. This superfamily contains five families par animals. (1) Listrophoridae, the half-clasping mites of small mammals, (gesidae, the feather mites of birds, (3) Cytoleichidae, parasites of the tissue (4) Canestriniidae, parasites of insects and (5) Sarcoptidae, the itch and mar

Rumex crispus—Curly dock	leaves
Ruta graveolens—Rue	leaves
Sanguinaria canadensis—Bloodroot	juice from stem and rootstock
Sedum acre—Mossy stonecrop	juice
Trifolium hybridum—Alsike clover	leaves
Urtica spp—Stinging nettles	hairy leaves and stems
Veratrum viride—Green hellefore	leaves

Most poisonous plants are harmful only when they are eaten. Relatively few plants produce poisoning by contact. The poisoning may consist of minor or temporary irritation of the skin or a painful irritation and inflammation with vesicles or blisters. Such a cutaneous disease or dermatitis may last only a few days or it may persist for weeks, depending on the severity of the infection and the susceptibility of the affected person By far the commonest cause of plant dermatitis in the United States is poison ivy, *Rhus toxicodendron*, and its closely related forms known as poison oak. The poison sumac, *Rhus vernix*, in the North, and poisonwood, *Metopium toxiferum*, in the extreme South, produce similar and even more severe dermatitis The parsnip, *Pastinaca sativa*, lady-slippers, *Cypripedium spp*, spurges, *Euphorbia spp.*, and the cultivated primrose, *Primula obconica*, are other common or widely distributed plants producing a number of cases of dermatitis

The dermatitis due to these plants is exemplified by the fact that the face, hands, forearms and genitals in men are the parts most commonly affected In men and in children there usually is a history of having handled the poisonous plant. In women the disease may occur on almost any part of the body and there may not be a history of direct contact, although there may be a history of handling pets that have come in contact with the poisonous plant The lesions, which vary greatly in size, are extremely numerous, thin-walled, closely aggregated, unruptured vesicles on inflamed bases When they affect the eyelids, the eyes become swollen closed. There are intense itching and burning

Some persons possess natural immunity In those who are susceptible the attacks will be repeated with each contact with the poisonous plant The disease is not contagious The prognosis in the individual attack is good

Plants Causing Photosensitization (Photodynamic Plants). Recently it has been shown that the toxic action of St.-Johns-wort, buckwheat, and several other plants is influenced by light These plants appear to contain substances which, when eaten by domestic animals, sensitize the animals to light so that serious symptoms may develop when the animals are exposed to strong sunlight Plants that sensitize animals to light by substances not normally present in the animal system have been designated as having a photodynamic action

Before photosensitization of an animal can take place as a result of eating a plant, certain conditions must be fulfilled (1) The animal must be white or have an unpigmented skin; otherwise the pigmented skin or dark fur or hair may screen out certain light rays (2) The animal must ingest the plant in question in sufficient quantity to supply the photodynamic substance (3) The animal must be exposed to bright sunlight subsequent to feeding on the plant.

If any one of these conditions is not met, symptoms may fail to develop.

The intricate relationships between sunlight and these cutaneous diseases in animals and man produced by certain plants, for example, fagopyrism by buckwheat and hypericism by St -Johns-wort, are complex and not well known

Food Poisoning From Plants. *Favism,* occurring mainly among Italians, is attributed to eating the fava bean or smelling the blossoms of the bean plant

Many cases of this disease in the United States are probably not recognized. Although there appears to be a hereditary basis for sensitization to this plant, the symptoms follow a definite pattern peculiar to this specific type of poisoning Indi-

Delphinium ajacis—Larkspur	leaves, seeds
Dictamnus albus—Gas-plant	seed pods, leaves
Dirca palustris—Leatherwood	bark
Echium vulgare—Vipers bugloss	leaves and stems
Encelia californica	leaves
Erigeron canadensis—Fleabane	leaves
Euphorbia marginata—*Snow-on-the-mountain*	*milky juice* *
Euphorbia corallata—Flowering spurge	milky juice
Euphorbia cyparissias—Cypress spurge	milky juice
Euphorbia esula—Leafy spurge	milky juice
Euphorbia helioscopia—Sun spurge	milky juice
Euphorbia peplus—Petty spurge	milky juice
Euphorbia lathyrus—Mole-plant	milky juice
Euphorbia ipecacuanhae—Spurge	milky juice
Fagopyrum esculentum—Buckwheat	leaves
Gelsemium sempervirens—Yellow jessamine	leaves and stems
Ginkgo biloba—Maidenhair-tree	fruits
Hedera helix—English ivy	leaves
Helleborus niger—Christmas-rose	leaves
Heracleum lanatum—Cow-parsnip	leaves
Hippomane mancinella—Manchineel	juice
Humulus lupulus—Hop	leaves
Hypericum perforatum—St.-Johns-wort	leaves
Iris versicolor—Iris	rhizomes
Iris spp.—Iris	rhizomes
Iva xanthifolia—Marsh-elder	leaves
Jatropha stimulosa—Spurge nettle	leaves and stems
Juniperus virginiana—Juniper	leaves
Laportea canadensis—Wood nettle	hairy leaves and stems
Leonurus cardiaca—Motherwort	leaves
Lobelia inflata—Lobelia	leaves
Maclura pomifera—Osage-orange	milky juice
Mentzelia oligosperma—Prickly herb	hairy leaves
Mentzelia ornata—Prickly herb	hairy leaves
Metopium toxiferum—Poison-wood	leaves, bark, etc.*
Nerium oleander—Oleander	leaves
	hairs on leaves and stems *
	leaves
	leaves
	leaves
	leaves
Phacelia minor—Prickly leaf pond weed	leaves
Phacelia pedicellata—Prickly leaf pond weed	leaves
Podophyllum peltatum—May-apple	rootstocks
Polygonum hydropiper—Smartweed	leaves
water pepper	leaves
	leaves
	leaves
	leaves *
Primula auricula—Primrose	leaves
Primula reticulata—Primrose	leaves
Primula sinensis—Primrose	leaves
Primula malacoides—Primrose	leaves
Tall field buttercup	leaves
p	leaves
	leaves
	leaves
Rhus toxicodendron—Poison ivy	leaves, bark, fruits *
Rhus quercifolia—Poison oak	leaves, bark, fruits *
Rhus diversiloba—Poison oak	leaves, bark, fruits *
Rhus vernix—Poison sumac	leaves, bark, *fruits* *
Rhus verniciflua—Japanese varnish-tree	leaves, bark, fruits and lacquer *
Rumex acetosella—Sheep sorrel	leaves
Rumex acetosa—Sour dock	leaves

* The most troublesome species.

Rumex crispus—Curly dock	leaves
Ruta graveolens—Rue	leaves
Sanguinaria canadensis—Bloodroot	juice from stem and rootstock
Sedum acre—Mossy stonecrop	juice
Trifolium hybridum—Alsike clover	leaves
Urtica spp.—Stinging nettles	hairy leaves and stems
Veratrum viride—Green hellefore	leaves

Most poisonous plants are harmful only when they are eaten Relatively few plants produce poisoning by contact. The poisoning may consist of minor or temporary irritation of the skin or a painful irritation and inflammation with vesicles or blisters. Such a cutaneous disease or dermatitis may last only a few days or it may persist for weeks, depending on the severity of the infection and the susceptibility of the affected person By far the commonest cause of plant dermatitis in the United States is poison ivy, *Rhus toxicodendron*, and its closely related forms known as poison oak. The poison sumac, *Rhus vernix*, in the North, and poisonwood, *Metopium toxiferum*, in the extreme South, produce similar and even more severe dermatitis The parsnip, *Pastinaca sativa*, lady-slippers, *Cypripedium spp*, spurges, *Euphorbia spp*, and the cultivated primrose, *Primula obconica*, are other common or widely distributed plants producing a number of cases of dermatitis.

The dermatitis due to these plants is exemplified by the fact that the face, hands, forearms and genitals in men are the parts most commonly affected In men and in children there usually is a history of having handled the poisonous plant. In women the disease may occur on almost any part of the body and there may not be a history of direct contact, although there may be a history of handling pets that have come in contact with the poisonous plant The lesions, which vary greatly in size, are extremely numerous, thin-walled, closely aggregated, unruptured vesicles on inflamed bases. When they affect the eyelids, the eyes become swollen closed. There are intense itching and burning.

Some persons possess natural immunity In those who are susceptible the attacks will be repeated with each contact with the poisonous plant. The disease is not contagious. The prognosis in the individual attack is good

Plants Causing Photosensitization (Photodynamic Plants). Recently it has been shown that the toxic action of St-Johns-wort, buckwheat, and several other plants is influenced by light These plants appear to contain substances which, when eaten by domestic animals, sensitize the animals to light so that serious symptoms may develop when the animals are exposed to strong sunlight Plants that sensitize animals to light by substances not normally present in the animal system have been designated as having a photodynamic action

Before photosensitization of an animal can take place as a result of eating a plant, certain conditions must be fulfilled (1) The animal must be white or have an unpigmented skin; otherwise the pigmented skin or dark fur or hair may screen out certain light rays (2) The animal must ingest the plant in question in sufficient quantity to supply the photodynamic substance. (3) The animal must be exposed to bright sunlight subsequent to feeding on the plant.

If any one of these conditions is not met, symptoms may fail to develop.

The intricate relationships between sunlight and these cutaneous diseases in animals and man produced by certain plants, for example, fagopyrism by buckwheat and hypericism by St.-Johns-wort, are complex and not well known

Food Poisoning From Plants. *Favism*, occurring mainly among Italians, is attributed to eating the fava bean or smelling the blossoms of the bean plant.

Many cases of this disease in the United States are probably not recognized Although there appears to be a hereditary basis for sensitization to this plant, the symptoms follow a definite pattern peculiar to this specific type of poisoning. Indi-

vidual susceptibility varies, and certain persons, after years of eating the beans with immunity, suffer a single severe attack and none subsequently. Ingestion of the beans by immune mothers may affect nursing infants There is no sex predilection

When fields of fava beans are in blossom, the inhalation type of the disease is most prevalent. The pollen is said to be sticky and is not widely disseminated. The first symptom appearing after inhalation of substances originating from the flowers or plant of the fava bean is dizziness, sometimes reaching the stage of collapse. This may occur within a few minutes or some hours after exposure and is usually followed by the gradual appearance of headache, malaise, and nausea. Repeated yawning, vomiting, chill, pallor, and pain in the lumbar region are followed by high fever. The most specific symptom is hemoglobinuria, which occurs within 5 to 40 hours, and is followed by icterus

Mushroom poisoning follows the eating of poisonous mushrooms which have been gathered in the woods and fields and mistaken for edible varieties. The poison is muscarine, a syrupy, alkaloid-like substance, which has been obtained in a crystallizable form as a hydrochloride from the mushroom *Agaricus muscarius* In its action it resembles pilocarpine, which stimulates the myoneural junctions.

There are some 70 to 80 species of mushrooms that are poisonous to man Emigrants from southern Europe to this country often confuse the poisonous ones with the European edible varieties The differentiation of the various types of mushrooms is a matter for a trained mycologist and not for the layman. The layman should not depend on the knowledge that he has gained from reading a book as being an accurate guide for him to select edible mushrooms in the woods

Symptoms often appear within 15 minutes after the mushrooms are eaten, but sometimes are delayed from 1 to 6 hours. This poisoning is characterized by salivation, excessive perspiration, a flow of tears, nausea, retching and vomiting, pain in the abdomen, and violent movements of the intestines which cause profuse watery evacuations The pupils are contracted Respiration is often quickened and dyspneic. Dizziness and confusion of ideas, coma and death may follow within 48 hours. In fatal instances there are fatty infiltration of the liver with central necroses, epithelial necrosis of the kidneys, acute enteritis, and colitis. The uremic condition resulting from the renal damage may be responsible for the symptoms.

Acute mushroom poisoning is treated by immediate gastric lavage followed by the instillation of a solution of starch into the stomach. The immediate intravenous administration of 5 per cent dextrose solution (1,000 ml.) is necessary Opiates may alleviate the distress Sometimes atropine or strychnine is employed.

The *water hemlock, Cicuta maculata,* is often erroneously called parsnip, wild parsnip, or wild carrot Its habitat is in swamps and meadows. The poisonous component of *Cicuta* is a resin.

In from 1 to 3 hours after ingestion of the leaves, flowers or roots there ensue nausea, vomiting and, in some, convulsions. Recovery occurs within a day or two

Country folk know that *rhubarb leaves* are poisonous and refrain from using them as a food, but since these leaves are occasionally so used by the uninformed, the United States Department of Agriculture has issued a warning to housewives against using this portion of the plant for food. Within a short time after ingestion there are cramplike pains in the abdomen which continue intermittently for a period of 36 hours or longer Death may follow.

Milk Sickness. Milk sickness is an intoxication caused by ingestion of milk and milk products of cows that have eaten white snakeroot (*Eupatorium urticaefolium*) or rayless goldenrod (*Aplopappus heterophyllus*) which are found in the central states of the United States, and jimmy weed (*Aplopappus heterophyllus*), found in certain sections of western Texas, New Mexico, and Arizona. Cattle apparently will eat these weeds when grazing is scarce The poison in snakeroot is due to a secondary alcohol, trematol ($C_{16}H_{22}O_3$). The primary intoxication in the animals is known

as "trembles" or "split tail" If the milk is drunk or if milk products are consumed by man from an affected cow, milk sickness ensues Pasteurization does not destroy the poisonous properties of the contaminated milk, butter or cheese.

In the acute form, the symptoms are anorexia, weakness, fatigability, constipation, nausea and retching; in the relapsing and probably in the chronic forms, the symptoms are nausea and vomiting There is a great thirst. The cheeks are flushed, and there may be a marked redness of the lips and tongue. The breath has a distinct odor of acetone The temperature is normal or subnormal despite the flushed appearance of the lips and cheeks. There are widespread muscular soreness and pain on palpation There is no increase in leukocytes The urine is scanty and contains acetone In fatal instances coma and convulsions precede death

Treatment should be directed toward the correction of the dehydration and acidosis. Empirically, as often predicated by folk medicine, the use of intoxicating doses of alcohol apparently improves the prognosis. Convalescence is prolonged, and relapse may follow premature physical exertion In patients who recover, weakness persists for days, weeks, or even months, depending on the initial severity of the illness

Honey Poisoning. A poison may rarely appear in the honey derived from certain nectar-bearing plants such as varieties of azalea, rhododendron, oleander, mountain laurel (*Kalmia latifolia*), palmetto, black locust, yellow jasmine (*Gelsemium sempervirens*) and species of *Andromeda, Leucothoe*, and *Pieris* belonging to the family Ericaceae

In the lay mind bitter honey may be considered as poisonous This is not true. For instance, the slightly bitter honey from dog fennel (*Anthemis cotula*) is delicious and not poisonous

The symptoms of honey poisoning begin immediately after the honey is eaten. There are tingling of the hands and feet, nausea and uncertainty of gait. If attempts are made to walk, the patient falls Headache may be severe. For several hours there is inability to rise Vomiting and severe diarrhea ensue The patient may become irrational and lose the senses for several hours All symptoms except weakness pass away in 24 hours

The diagnosis is made from a history of eating comb honey The comb honey, according to folklore, may be tested by feeding some of it to a dog. If the honey is poisonous, symptoms appear in the dog within one-half hour.

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21

THE PHYSICAL EFFECTS OF HEAT AND COLD ON THE BODY AS A WHOLE

BODY TEMPERATURE

Thermal control of the body depends on balanced autonomic nerve centers situated in the diencephalon The center of control of body cooling is in the posterior hypothalamus. The center for control of overheating seems to be located near the supraoptic and paraventricular nuclei Owing to the thickness of the scalp and calvarium the cranium and its contents are effectively insulated and the heat regulatory centers are rarely affected by the temperature of the environment of the head These regulatory centers are sensitive to changes in temperature and chemical composition of the arterial blood Additional factors in thermal controls are endocrine and autonomic-sympathetic reflex vasomotor responses

Physiologic regulation of body temperature consists of balancing heat production and heat loss Heat production is subject to pituitary, adrenal and thyroid control and the availability of nutritional substances. The rate of heat production can increase by 10 times during heavy work It can rise from 4 to 8 times, without exercise, merely by the onset of shivering Heat loss is achieved through the skin and the lungs The amount lost through expired air depends on the temperature, density and humidity of the air, as well as on the respiratory rate and depth. The amount of heat lost from the cutaneous surface (radiation, conduction, convection and evaporation of water) depends on the relative degree of vascular dilatation of surface and near-surface blood vessels, and on other factors such as pilomotor response and function of sweat glands The amount of heat lost from skin and lungs by evaporation of water is relatively greater at low environmental temperatures than at high environmental temperatures

Normal Limits. The normal temperature of the body varies within narrow limits. The average is 98 6 F (37 C) Any temperature from 97.2 to 99 0 F may be considered to be within proper boundaries, although these may be normally exceeded for short periods of time. The temperature is modified somewhat by age, the temperature of the newborn infant ranging from 99 to 99 7 F; while between 60 and 70 years of age it may vary from 99 7 down to 97 F. Violent exercise, especially in warm weather, will raise the temperature to a slight extent. Mental exertion or excitement may raise it to a moderate degree (100 4 F).

The most nearly constant normal variation is that which occurs diurnally. Under ordinary circumstances the temperature is highest between 5 P.M. and 8 P.M., and lowest between 2 A M and 6 A.M The influence of this rhythmical change of temperature is seen in many fevers In those who work by night and sleep by day this type is reversed. The temperature may rise 0 4 F after a meal, the so-called fever of digestion The readings of the thermometer differ somewhat according to the cavities in which it is placed It is to be remembered that the mean temperature of the

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air, (2) its moisture content, (3) air movement and (4) radiation transfer between the body and its immediate environment. The *temperature* of the body and the air is expressed as the dry bulb temperature.

Through the efforts of the United States Public Health Service, the United States Bureau of Mines, and the Research Laboratory of the American Society of Heating and Ventilating Engineers, as recorded by Ferderber and Houghten, not only have the effects of these four environmental factors in controlling heat exchange between the body and the atmosphere been evaluated but these factors have been combined into a single comfort index known as the effective temperature. This scale takes into account the temperature of air, its moisture content and its movement. It has been shown that this effective temperature index, particularly in hot atmospheres, is a true measure not only of a person's feeling of warmth but of many of the physiologic reactions, including changes in body temperature, increase in pulse rate and change in leukocyte count of the blood

The average person at rest is ideally comfortable at about 66 F effective temperature during the winter season, but in a summer-cooled space ideal comfort is attained at about 72 F effective temperature This may be observed with 75 F dry bulb at 70 per cent relative humidity, or 80 5 F dry bulb at 30 per cent relative humidity. Most persons would be uncomfortably warm and perspiring at an 85 F effective temperature irrespective of the moisture content Most persons seated at rest will maintain temperature equilibrium with profuse perspiration in an effective temperature as high as 89 F. At higher effective temperatures equilibrium of body heat will not be maintained, body temperature will rise and pulse rate will increase as the effective temperature increases, so that in a condition of 92 5 F effective temperature the average person will have a rise of 1 7 F in body temperature and an increase in pulse rate of 48 per minute in 3 hours. The same physiologic changes will occur at an effective temperature of 96.5 F and 20 per cent relative humidity when the dry bulb is 131 F, or 32 F above body temperature, as would occur in 96 5 F effective temperature with a high relative humidity of about 90 per cent when the dry bulb temperature is only 99 F, or approximately the same as the body temperature

Physiologic reactions follow the effective temperature index rather than the dry bulb temperature As an example, Simpson has shown that induced fever therapy will give a rise in body temperature to 105 F in from 40 minutes to an hour with a dry bulb temperature ranging from 130 to 150 F and a relative humidity from 35 to 50 per cent However, Houghten, Ferderber and Gutberlet have shown that in a saturated atmosphere the same rise in body temperature will occur in about the same time with a dry bulb temperature of approximately 113 F

Air-Conditioning Shock. The discomfort on emerging during the summer season from a cooled, air-conditioned space into natural atmosphere and the reverse has been made the basis of many complaints against air conditioning. There has come into use the term air-conditioning shock, and unfavorable comment has been made that such swift changes promote respiratory diseases

Mudd, Goldman and Grant demonstrated that chilling of the body surface of human beings causes reflex vasoconstriction and ischemia in the mucous membranes of the nasal cavity and the postnasal space They expressed the belief that this ischemia might cause a lowering of the local resistance, which would allow infection to occur. During the course of their experiments, 10 of the subjects developed acute colds and sore throats, and a change in the bacterial flora was demonstrated.

Workers in mines in which the temperature constantly is at 56 F, on leaving such a mine to enter a natural atmospheric temperature, at times of 96 F, may immediately suffer from dizziness, quick fatigue, profuse sweating, flushing of the skin, syncope and other manifestations suggesting cardiovascular weakness evidenced by a quick lowering of the blood pressure

It is difficult to correlate the foregoing experiences with the number of degrees of change in the environmental temperature, for during the winter season it is not extraordinary to pass from an outside temperature at 0 F into a warm room of 80 F.

Fahrenheit and divide by 1 8 *Conversely, to convert from Centigrade to Fahrenheit* multiply by 1 8 and add 32.

The temperature is recorded by either Fahrenheit or Centigrade thermometer placed in the mouth, axilla, rectum, vagina, or *the fold of the groin* The *temperature* of the urine is sometimes tested in a male suspected of malingering.

If the mouth is employed, neither a very hot nor a very cold drink should have been taken for half an hour before.

It is more accurate to use the rectum or the vagina than the mouth. The thermometer is oiled and introduced to the depth of 2 inches. The rectum must be empty of feces *The temperature may also be taken by the rectum in those who are* being tubbed, and when there is doubt as to a recorded reading or a suspicion of malingering

The *surface temperature is taken by a self-registering thermometer, the base of* which has been flattened or coiled so as to present a relatively large surface for contact with the skin.

In ordinary cases the temperature should be taken if possible morning and night, preferably at the same hour each day If in a private home a professional nurse is not on duty, it is possible to instruct a member of the family in the procedure *or to furnish extra thermometers on which the temperatures are recorded* at specified times and which are then laid aside for reading on the next call

In a report of the Council on Physical Medicine and Rehabilitation on oral and *rectal temperatures of man, Horvath, Menduke and Piersol commented that the* so-called normal body temperature of a healthy person has been stated categorically to be 98 6 F (37 0 C), and repeated the clinically accepted truism that the *rectal temperature is 1 F higher than the oral, or approximately* 99 6 F (37.6 C). These values have as their basis the present-day standard of 98.6 F which originated from the work presented long ago by Becquerel and Breschet, and by Wunderlich *who, working separately, found the mean oral temperature* to be 98 6 F The range of the means reported is from 97 2 to 99 0 F.

Horvath, Menduke and Piersol made a controlled study on normal men and women. *The mean of the temperature for men in the morning* was 98.2 F; the mean for the women in the morning was 98 6 F The difference was 0.4 F The standard error of this difference was 0 15 F. In addition to having a higher mean temperature, women exhibited greater variability in their mean temperatures than did men

The difference between the rectal and oral temperatures for men was 0 84 F, for women, 0.76 F The mean range of rectal temperatures in men was 1.2 F and in women 1.5 F. The mean range of differences between rectal and oral temperatures was 1 0 F for men and 1 4 F for women.

Both men and women had a significantly higher mean evening rectal temperature than a mean morning rectal temperature There is no single "normal" temperature value for all men. Neither is there a single "normal range" of temperature for all men These statements are equally true with respect to the differences be-

on the destructive metabolisms, mainly processes of oxidation, which are constantly going on throughout the tissues of the body. The skeletal muscles and the glands, especially the liver, constitute the chief seats of heat production.

Heat dissipation (thermolysis) takes place mainly through the expired air, and by conduction, convection, radiation, and evaporation from the skin. *Since from* 77 to 85 per cent of the total heat lost passes off from the cutaneous surface, the skin must be considered as the principal factor in heat dissipation.

There are four factors in the atmospheric environment *which affect* loss of heat from the body in the following order of importance: (1) the temperature of the

air, (2) its moisture content, (3) air movement and (4) radiation transfer between the body and its immediate environment. The *temperature* of the body and the air is expressed as the dry bulb temperature

Through the efforts of the United States Public Health Service, the United States Bureau of Mines, and the Research Laboratory of the American Society of Heating and Ventilating Engineers, as recorded by Ferderber and Houghten, not only have the effects of these four environmental factors in controlling heat exchange between the body and the atmosphere been evaluated but these factors have been combined into a single comfort index known as the effective temperature. This scale takes into account the temperature of air, its moisture content and its movement. It has been shown that this effective temperature index, particularly in hot atmospheres, is a true measure not only of a person's feeling of warmth but of many of the physiologic reactions, including changes in body temperature, increase in pulse rate and change in leukocyte count of the blood

The average person at rest is ideally comfortable at about 66 F effective temperature during the winter season, but in a summer-cooled space ideal comfort is attained at about 72 F effective temperature This may be observed with 75 F dry bulb at 70 per cent relative humidity, or 80 5 F dry bulb at 30 per cent relative humidity Most persons would be uncomfortably warm and perspiring at an 85 F effective temperature irrespective of the moisture content. Most persons seated at rest will maintain temperature equilibrium with profuse perspiration in an effective temperature as high as 89 F. At higher effective temperatures equilibrium of body heat will not be maintained, body temperature will rise and pulse rate will increase as the effective temperature increases, so that in a condition of 92 5 F effective temperature the average person will have a rise of 1.7 F in body temperature and an increase in pulse rate of 48 per minute in 3 hours. The same physiologic changes will occur at an effective temperature of 96 5 F and 20 per cent relative humidity when the dry bulb is 131 F, or 32 F above body temperature, as would occur in 96 5 F effective temperature with a high relative humidity of about 90 per cent when the dry bulb temperature is only 99 F, or approximately the same as the body temperature

Physiologic reactions follow the effective temperature index rather than the dry bulb temperature As an example, Simpson has shown that induced fever therapy will give a rise in body temperature to 105 F in from 40 minutes to an hour with a dry bulb temperature ranging from 130 to 150 F and a relative humidity from 35 to 50 per cent However, Houghten, Ferderber and Gutberlet have shown that in a saturated atmosphere the same rise in body temperature will occur in about the same time with a dry bulb temperature of approximately 113 F

Air-Conditioning Shock. The discomfort on emerging during the summer season from a cooled, air-conditioned space into natural atmosphere and the reverse has been made the basis of many complaints against air conditioning. There has come into use the term air-conditioning shock, and unfavorable comment has been made that such swift changes promote respiratory diseases.

Mudd, Goldman and Grant demonstrated that chilling of the body surface of human beings causes reflex vasoconstriction and ischemia in the mucous membranes of the nasal cavity and the postnasal space They expressed the belief that this ischemia might cause a lowering of the local resistance, which would allow infection to occur During the course of their experiments, 10 of the subjects developed acute colds and sore throats, and a change in the bacterial flora was demonstrated.

Workers in mines in which the temperature constantly is at 56 F, on leaving such a mine to enter a natural atmospheric temperature, at times of 96 F, may immediately suffer from dizziness, quick fatigue, profuse sweating, flushing of the skin, syncope and other manifestations suggesting cardiovascular weakness evidenced by a quick lowering of the blood pressure.

It is difficult to correlate the foregoing experiences with the number of degrees of change in the environmental temperature, for during the winter season it is not extraordinary to pass from an outside temperature at 0 F into a warm room of 80 F.

Thus a differential of 80 F occurs without profound discomfort either then or soon thereafter. However, the person who enters a warm building from an outside temperature of 0 F or thereabouts removes the overcoat, mittens, overshoes and headdress.

Fever. Fever is a condition indicated by a more than transient rise of body temperature There is implied a disturbance of the normal relation between heat production and heat dissipation, from causes acting on one or the other, or on the heat-regulating mechanism. Heat production in fever is largely increased because of increased rapidity of destructive processes which take place in the body, as evidenced by the larger than normal amounts of urine and carbon dioxide which are excreted, and the larger quantity of oxygen which is consumed. Increased formation of heat alone, however, may not be sufficient to account for the increase of body temperature unless the increased formation of heat is excessive or the loss of heat to the immediate environment is hampered In fever, therefore, it is necessary to assume a disturbance of the thermotaxic mechanism, and this perturbation of heat regulation is perhaps the most characteristic element in the production of fever heat Fever is a complex process or condition of which the presence of an elevated temperature is the most significant and practical indication

In general, fever is caused by or attends, (1) all inflammations, acute, subacute or chronic, the great majority of which are recognized as being dependent on the presence of microscopic or ultramicroscopic organisms in the inflamed area, whence toxic material enters the general circulation, (2) toxemias resulting from the injection or ingestion of toxic or poisonous material or the absorption of toxic or poisonous material from the digestive tube; (3) the formation of toxic aseptic material from the tissue with subsequent absorption, (4) the contact with certain allergins by those who have an allergic state; (5) hemolysis (hemolytic crisis) in certain blood dyscrasias, (6) some instances of disease of the central nervous system (disease or injury to the cerebral cortex, hypothalamic region and spinal cord) in which the heat-regulating mechanism presided over by the autonomic nervous system is interfered with by direct or reflex causes, (7) some instances of advanced malignant lesions, either sarcomas or carcinomas but more commonly the former; (8) dehydration and (9) starvation

An overheated room and the ingestion of food may cause a rise in temperature

Fever may be caused by injury to the upper part of the cervical portion of the spinal cord or by excessive increases in intracranial tension, and terminally in brain tumors An unusually cool room, cold sponging, and the cold tub are fever-reducing agents. If a slow loss of blood occurs, as when menstruation takes place during fever, the temperature is lowered to some extent, and a large, sudden hemorrhage may cause a drop below the normal Persistent subnormal temperature may be present in connection with convalescence from fevers, in acute alcoholism, melancholia, myxedema, starvation (sometimes elevated), wasting diseases, and in various kinds of poisoning Locally, abnormal coldness of an edematous or cyanosed part may be observed

The febrile reaction is characterized by increase in pulse rate (100 to 160 per minute). The cardiac output is increased and the circulation time is decreased. After the chill, if there should be one, there is an extensive vasodilatation in the skin but the decrease in peripheral resistance is well balanced by the increased cardiac output During fever the heart is subjected to strain The systolic blood pressure is usually increased while the patient is in the recumbent position but lowered, in the erect position The greater changes may occur in the diastolic blood pressure, which may become impossible to determine by the ordinary means, particularly in the upright position This decrease in the diastolic blood pressure may weaken the heart from the effects of reduction in the blood pressure.

In a chill associated with an elevated temperature, the surface of the body is

cold and pale. The teeth chatter, the lips and nails are cyanotic, and the skeletal muscles rapidly contract and relax. The fever may reach its highest point during the chill

Many of the symptoms attributed to infections are really the manifestations of fever The symptoms of fever are due partly to tissue changes, partly to increased heat of the body, and partly to functional disturbances of affected organs or tissues Besides the abnormal rise of temperature, these symptoms are: ill feelings, or malaise; sleeplessness; thirst; loss of appetite, mental disturbance, amounting to delirium in excessive fever; increased frequency of pulse and respiration· lessened amount of urine; usually headache and backache; and, if the fever is long-continued, general wasting of the body. There is also likely to be nausea and constipation, and a chill may initiate or accompany a sudden rise of temperature.

The symptoms accompanying fever exhibit considerable variations in severity according to the character and the cause of the fever, and the duration and height of the pathologic temperature There is also a difference in the enduring power of individual patients, more easily recognized than explained, which with equal temperatures and apparently similar causes will allow one patient to continue about his daily work with slight subjective symptoms and will send another to bed in a condition of extreme weakness and discomfort The malaise may be slight or marked. Thirst and dryness of the mouth, together with anorexia, epigastric discomfort and nausea on taking food, and constipation, are due to varying degrees of suppression of the digestive secretions The total fluid intake is often diminished in quantity, the urine is scanty and high colored The pulse rate, as a rule, is increased. However, in meningitis, influenza and typhoid fever the pulse may be slowed. In infections generally the pulse rate and the respirations increase.

Backache, headache, and aching of the limbs are nearly always present, but there is considerable variation in their severity As a rule, they are most marked at the beginning and, as in some of the acute infectious diseases, may possess distinct diagnostic value because of their prominence as symptoms The headache of the rickettsial infections and the backache of variola are examples The mental disturbances of fever may be manifested by an increased activity of the mind, passing into active delirium, or by mental torpor, deepening into a low muttering delirium. The degree or character of the delirium or mental disturbance does not appear to depend entirely on the height of the temperature, but rather on the nature and amount of the toxins circulating in the blood and their effect on the nervous system. Personal idiosyncrasy and age modify the liability to the occurrence of delirium.

Fever temperatures are referred to according to type and height The terms employed to designate the types of fever are self-explanatory For example, there are continued, remittent, intermittent, recurring, and irregular fevers

If a fever ends by a sudden drop of the temperature to or below the normal, the termination is by *crisis*, and is usually accompanied by profuse sweating and an increased flow of urine

If the decline of the fever is slow and gradual, several days elapsing before the temperature reaches normal, the termination is by *lysis*

A temperature below 97 2 F is subnormal, and 95 F is the temperature of collapse.

Changes in the temperature are much more easily produced when it is already abnormal Consequently, if fever exists, agencies which in health would cause little or no alteration in the temperature will give rise to marked oscillations of the temperature If hourly temperature recordings are made for 24 hours, in almost any case of fever, irregularities will be revealed which cannot be explained by past events or future developments

A rise of temperature to an unusual height, 107 to 110 F, is termed hyper-

pyrexia, which may develop in connection with malarial intermittent or remittent fever, rickettsial infections, hepatitis, sunstroke, tetanus, typhoid fever, yellow fever, and shortly before death from any cause, but particularly in brain tumors. It may also result from trickery by the use of friction, pressure, hot water bags, poultices or inverted shaking of the thermometer.

Localized rise of temperature, except in surgical diseases, is not of great diagnostic importance. The local heat of the surface is increased over a pneumonic lung, and there may be a rise in temperature in areas affected by vasomotor paralysis.

EFFECT OF HEAT ON THE BODY

The injuries to the skin by heat may be primarily induced by contact with hot objects or the skin may be hypersensitive or allergic to heat

The application of heat to the skin or mucous membranes by liquids, solids, flame, steam and radiant heat causes burns These burns are classified as. *first degree* burn manifested by reddening of the outside layers of the skin; *second degree* burn exhibiting blebs and vesicles, *third degree* burn denoting destruction of the skin and often subcutaneous and other superficial tissues First and second degree burns leave no scars

A first degree burn covering a large area, a second degree burn covering a smaller area and a third degree burn covering a limited area of the body surface may cause shock, to be followed by fever, fast pulse and often vomiting and diarrhea Blood may occur in the excreta as the result of a gastroduodenitis or duodenal ulcer (Curling's ulcer) The duodenitis and ulcer may be due to an acute insufficiency of the adrenocortical hormones

Hematuria, granular and blood casts may signify the presence of a lower nephron nephrosis

The toxemia which follows extensive first or second degree burns as well as the toxemia of third degree burns is due to (1) fluid loss (salt and water), (2) oxygen deficiency and (3) adrenal insufficiency.

The diagnosis of burns is obvious. The difficulty may lie in the determination of whether or not the patient had at the time of the burn another disease which caused the loss of postural balance or mental alertness which permitted him to sustain the burn

In the *rescue from distress caused by heat*, the survival time is a less decisive factor than the span of time in which man is still able to act, the escape time. Incapacitation occurs when the average body temperature rises by as little as 1 C.

If *death has occurred in a fire* the blood will almost invariably show a high concentration of carbon monoxide. In addition, particles of soot are usually present on the mucosae of the larynx, trachea and bronchi The presence of true blisters, or of a peripheral zone of hyperemia, associated with burns of the skin indicates life at the time the burns were sustained If death occurred in the fire, analysis of the blood for ethyl alcohol may reveal that escape was rendered more difficult by inebriation Examination of the viscera and extremities will reveal whether injury or disease prevented escape. Certain postmortem artefacts of burned bodies produced by heat may be confused with premortem injuries. These artefacts include splits of the skin which simulate incised wounds, pseudoblisters caused by formation of steam beneath the epidermis, cracks of the outer table of the skull from drying and shrinkage, fractures of the entire thickness of the skull from the generation of steam in the cranial cavity, and epidural hematomas over the vertex of the brain.

Most deaths in conflagrations are due to heat, noxious gases (especially carbon monoxide) or the combined effects of heat and gases. Death from heat is indicated by extensive burns of the body, together with hemorrhages beneath the endocardium

of the septal surface of the left ventricle of the heart. Identification of partially burned bodies may be made from dental peculiarities or from individual physical characteristics, such as congenital abnormalities or residua of disease or surgical operation.

Overcharging of Heat Balance. Heat enters the body from a hot environment mainly through the skin and usually increases the peripheral blood flow. This effect causes an increased heat conductivity of the periphery and, therefore, an increase of temperature of the body. Profuse sweating, which usually commences a few minutes after exposure to heat may, through evaporation cooling, counteract the overheating with air temperatures up to 140 F In moist air this limit will be reached at temperatures less than 140 F. The more heat that enters the body, the greater the imbalance of physiologic factors, such as the temperatures of different parts of the body or of the circulatory system; finally signs of breakdown occur. The rise of the average body temperature seems to be a valuable indicator of this stress

The heat balance of the body seems to be somewhat improved by acclimation. Generally, however, the upper environmental limit in which a person can work is a dry bulb temperature ranging between 93 and 121 F and a wet bulb temperature ranging between 90 and 96 F At this upper environmental limit a narrow range of wet bulb temperature, 4 to 5 F, separates environments in which work is relatively easy from those in which work is impossible. When the wet bulb temperature is below 91 F work is easily and efficiently performed. Between 91 and 94 F wet bulb temperatures, prolonged moderately hard work is possible but efficiency is lost and work is difficult Vigor and alertness are lost Total disability occurs from moderately hard work at wet bulb temperatures of 94 F and higher. Work of a longer duration than 1 hour at these temperatures greatly decreases tolerance. At a dry bulb temperature of 120 F sweating is extremely profuse, averaging 2 to 3 liters per hour This is considered the upper environmental limit for the dry bulb temperature Above these upper environmental limits, there develop, even in acclimatized persons, severe physiological changes and undesirable, frequently disabling symptoms similar to those sustained by unacclimatized persons when working in the heat

There are three clinical syndromes which can be attributed to overcharging of the heat balance. These are (1) sunstroke, (2) heat exhaustion and (3) heat cramps.

Sunstroke. Sunstroke is distinguished from heat exhaustion and from heat cramps.

Exposure to the sun which may not be prolonged, or short exposures to excessive heat indoors, when the humidity of air is high, is the cause of sunstroke The excessive humidity is necessary, for in a dry atmosphere *heat exhaustion* is produced

Schickele made analyses in 198 cases of heat fatalities suffered by soldiers in training in the United States from 1942 to 1944. From these, 157 were selected in whom no cardiac or other disease which would predispose to increase in body temperature could be found, and in whom, therefore, if death occurred it might be presumed to be due only to the effects of exposure to heat Heat deaths were found to be caused by the heat load, as determined by climate, activity and body build "Rapid acclimatization" of 1 week or 10 days or even a month did not confer immunity to heat injury, for there were as many deaths in those who had had 4 weeks' exposure as in those who had had 1 week's exposure The mortality rate and incidence of sunstroke fell off rapidly after longer acclimatization periods Susceptibility to heat stroke appears to be particularly high among persons acclimated to an atmospheric cooling above a certain level (about 600 calories hourly per square meter of body surface) when they are exposed to an atmospheric cooling power reduced below this level

In death from sunstroke the brain is congested and petechial hemorrhages occur under the pia and in the floor of the third and fourth ventricles. Changes are found in the neurons, and degenerative changes in the glia cells are present

The symptoms commence with headache, thirst and vomiting after drinking water. Some may suffer diarrhea as a first symptom.

The skin is flushed and dry; consciousness is soon lost and the patient falls to the ground. Convulsions are frequent. Often there is present a critical and always *a serious elevation of temperature which may reach 110 F and never less than 104 F.* The pulse is quick and full, respiration is rapid and sometimes irregular. The pupils are first dilated and later contracted. As a rule, the muscles are flaccid but they may be rigid. In some patients ecchymoses or petechial hemorrhages are found over the body. In more favorable circumstances loss of consciousness lasts only a short time, but in fulminating instances signs of increased intracranial pressure, such as bradycardia and Cheyne-Stokes respiration, develop very rapidly and the patient may die within an hour. During convalescence there is severe headache. Memory is impaired and there are irritability, loss of emotional control, difficulty in concentration and irregularities of body temperature.

The spinal fluid is under increased pressure and shows a mild pleocytosis. There is usually a moderate percentage of polymorphonuclear cells present at first and often there are a few erythrocytes, but within a few hours lymphocytes are predominant.

The diagnosis of sunstroke is based on the history of exposure to extreme atmospheric heat and humidity in bright sunlight or elsewhere, followed by sudden headache, coma, dryness of skin and high temperature. In heat prostration there are, on the contrary, a subnormal temperature, pale, moist skin and small pulse; consciousness is usually preserved and there are usually no convulsions. Heat cramps give symptoms like those of tetany, in fact, this condition is probably a type of tetany due to depletion of the body chlorides.

The immediate mortality of sunstroke is very high. In mild instances complete and relatively rapid recovery may be expected, but after severe sunstroke, prolonged headache and psychic disturbances may be expected. Sometimes personality changes and an increased susceptibility to heat are permanent.

Heat Exhaustion. In contrast to sunstroke, heat exhaustion occurs *in hot dry weather or in hot dry climates, for instance, in the desert. In those who are conditioned to a hot dry climate two types of heat exhaustion occur.*

The *first type* of exhaustion occurs during the first part of the summer. There is a sodium chloride deficiency and dehydration. Chlorides in the plasma and whole blood are grossly diminished. There is evidence that this type of heat exhaustion occurs in those who habitually secrete sweat containing a higher concentration of chloride than the average. Their salt intake is inadequate for their excessive loss through the sweat.

The onset of the illness is generally with vomiting and muscular cramps.

On examination the patient is pale, collapsed and sweating. On attempting to stand, syncope ensues. The blood pressure is usually normal or low. The pulse pressure is consistently low. The urine is scanty, of high specific gravity, and almost devoid of chloride.

Diagnosis is based on the foregoing findings.

The *second type* of heat exhaustion occurs *late in summer in conditioned persons.*

These persons are salt deficient but not so much so as those who have the first type of heat exhaustion. During the long exposure to the heat it seems that the salt content of the sweat increases, so that they too excrete an excessive amount of salt.

The onset of the illness in these patients is not sudden as in the *first type.* There first appear the prickly heat, defective sweating and polyuria.

On examination there is a healing, desquamating prickly heat. The skin is moist, not dehydrated. There are no changes in blood pressure or pulse pressure. Chloride

content of the plasma is decreased but not so much as in the first type of heat exhaustion During convalescence sweat containing an increased chloride content is secreted.

Diagnosis is made on the foregoing findings. The aged and the debilitated are susceptible to heat exhaustion

Heat Cramps. Heat cramps or muscular cramps due to the effects of heat are a part *of the syndrome of heat exhaustion* (first type heat exhaustion). The affected person is not well conditioned to an excessive exposure to heat and severe muscular cramps ensue.

This type of heat injury was common during the era of steamships that were powered by coal-burning boilers. After a few hours in the boiler room, usually when the ship was making full speed ahead, in temperatures well above 100 F (110 to 120 F), the victim was suddenly seized with moderate to severe pains in anterior thigh and abdominal muscles

The examination of these patients rarely reveals any detectable abnormalities such as fever or blood pressure changes. The cramps soon cease on cooling of the body However, the individual is weak and unable to work for the following 1 or 2 days.

Hypersensitivity to Heat. Sensitivity to heat is created by a number of circumstances A most disabling sensitivity to heat is that which follows severe sunstroke and is manifested by various systemic reactions The milder forms of sensitivity to heat have been described by Duke as comprising three types of reactions. (1) reactions caused by an increase of calories regardless of the source; (2) reactions caused by local increase of temperature and (3) reactions caused by sensitivity to both heat and cold

Sensitivity to heat almost always begins after the age of 40 years. It is likely to follow an acute illness, or a person previously sensitive to heat may become free of symptoms during an acute febrile illness. This sensitivity is most commonly manifested by urticaria (see Chapter 18).

Erythermalgia (Erythromelalgia). Erythermalgia is a disease of unknown etiology which is characterized by an unusual sensitiveness of the skin to warmth. When erythermalgia occurs in association with hypertension, polycythemia vera, gout, certain organic diseases of the nervous system or heavy metal poisoning, it is termed secondary erythermalgia

As a rule, the symptoms commence in middle age or later in life in both men and women However, the disease has been observed in children The burning discomfort of the hands and feet which characterizes erythermalgia can be induced by warming the skin and can be maintained when the flow of blood has been brought to a standstill Direct pressure on the skin gives relief. The distress may localize to a small portion of an extremity, usually a foot It comes on when the patient is walking or after getting warm in the bed at night, and may be severe. It may last from a few minutes to several hours and is always *greater during hot* weather It may be relieved by cooling the extremity. Trophic changes, ulceration and gangrene do not occur in primary erythermalgia

Examination of the involved extremity during an attack reveals a painful red region of skin with an increased temperature The pulsations in the peripheral arteries are within normal limits.

The examination in the secondary form of the disease reveals diverse findings, depending on the nature of the primary disease.

The relationship of the episodes of distress to dependency and to relief by elevation and by applications of cold is helpful in making a diagnosis The final diagnosis is based on objective study of the temperature of the skin during an attack.

In the diagnosis of erythermalgia it is essential to demonstrate that the skin temperature and the distress *are related The extremity* may be enclosed within a

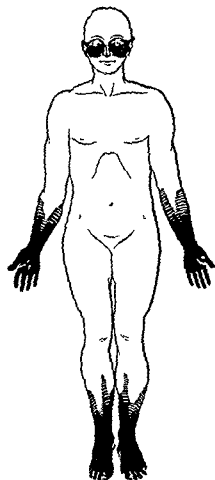
tent in which a lighted carbon filament bulb is placed, as soon as the extremity has been warmed sufficiently, the distress will supervene

There is no successful *treatment.*

Erythema Ab Igne *(Fire Shanks).* In fire shanks the skin over the lower anterior aspects of the legs is brown and of a motley appearance. The condition is found in persons habitually exposed to strong heat, such as engine drivers and those who use open fireplaces for heating the house in cold climates. After unduly cold winters in the South, where fireplaces are in common use, the disorder has been observed in both white and colored persons. The configuration of the pied patches is due to the penetrative power of the heat rays which causes dilatation of the deep arterioles and consequent congestion at the limits of the area supplied by each Dermatitis may result in severe cases if there is present an increased sensitivity to heat.

EFFECTS OF COLD

The skin reacts after exposure to cold by exhibiting an *erythema (erythema pernio)* Prolonged exposure to low temperatures causes a destruction of the skin and perhaps of the deeper parts as well, as seen in frostbite The destructive effects of cold are increased by dampness, as in trench foot or immersion foot



Redrawn from Coon, Garn and Birdsell Races, C C Thomas, 1950

Fig 21-1. Surfaces of the body most commonly injured by cold

Extremities having varicose veins or nerve injuries, or those which have been affected by anterior poliomyelitis or hemiplegia, are more susceptible to injury by cold than normal extremities Cold injuries of the skin are bilateral and usually symmetric unless there has been some irregularity of exposure or of nerve injury (Fig 21-1) In the latter case the lesion is more advanced on the previously injured extremity.

The disease syndromes manifested as the result of a cold environmental temperature are (1) pernio syndrome comprising acute pernio (acute chilblains) and chronic pernio (chronic chilblain erythrocyanosis), (2) excessive sensitivity to cold and heat, (3) immersion foot and (4) frostbite

These manifestations are due mainly to vascular injury by cold temperatures

Pernio Syndrome. The pernio syndrome includes *acute chilblain, chronic chilblain,* immersion foot and trench foot.

Acute Pernio. Acute chilblain or acute pernio affects children who are exposed to snowy cold wet weather without adequate protection for their feet and legs. Acute pernio on the shins is common in women who have inadequate protection of their legs while they are exposed to the cold. On returning to a warm room there is an intense itching and burning of the affected region Acute manifestations persist for several days; if lesions have not become infected, they gradually clear up in about a week or 10 days

The manifestations of a more severe acute pernio are characterized by derma-

titis in the affected regions which is bluish red and is associated with slight edema A residual brownish pigmentation persists for several weeks after an acute lesion has subsided. In rare instances a hemorrhagic, purpura-like reaction may appear in the affected region during the acute stage of the lesion. When this reaction appears or the lesion becomes infected, the condition may resemble a dermatitis from some other cause.

When the toes are affected, they burn and itch, and become reddish or cyanotic after exposure to cold. Swelling of the toes may occur and hemorrhagic blebs may supervene

Chronic Pernio (*Chronic Chilblain*) Synonyms for chronic pernio are erythrocyanosis, Bazin's disease, dermatitis hiemalis and lupus pernio.

On repeated exposure to cold, recurring and chronic cutaneous lesions develop which are erythematous, ulcerative and hemorrhagic and on healing leave scarring, fibrosis and atrophy of the skin and subcutaneous tissues The lesions usually clear up during the warm season. However, in some persons who are accustomed to an open fireplace these atrophic pigmented lesions of the skin become permanent, and this condition has been called fire shanks

Repeated vasospasm which is the result of reaction to cold may be responsible for the vascular changes in pernio As the result of vasospasm anoxemia changes in the tissue followed by chronic inflammatory reaction of varying extent and degree occur.

On examination the lower extremities are found cool and often slightly cyanotic and edematous Over the lower parts of the legs there may be many shallow ulcers of varying sizes Scars and pigmented spots from previous healed lesions may be observed The peripheral arteries are pulsating

The lesions of the active stage and a history of the influence of cold and change of season are rather characteristic of chronic pernio During a quiescent period the differentiation of erythema induratum, erythema nodosum and idiopathic nodular vasculitis will have to be made The differential diagnosis of these conditions may be impossible in occasional cases

Peripheral Vasoneuropathy After Chilling. Immersion Foot. Immersion foot is a term applied to a condition produced by long immersion of the feet in cold water, usually associated with immobility of the limbs and constriction by boots or other clothing An exactly similar condition may affect the gloved hands when exposed to water The essential cause of this disturbance is exposure of the limbs to cold insufficient to freeze the tissues. Immersion, according to Ungley and his associates, has no specific action apart from its effect in keeping the parts cold. Webster, however, expressed the belief that the condition may occur to those exposed for long periods in subtropical waters and thus it cannot be classed as a true frostbite.

The following factors influence the occurrence and severity of the injuries incident to immersion foot. (1) time of exposure and temperature of water; (2) footwear which, because of constriction, is harmful for long exposures; (3) immobility; exposed persons who keep moving suffer less than those who sit still; (4) chilling of the body from wind or from repeated wetting; and (5) inadequate clothing.

The immersed limbs become numb and clumsy and may be painful. As the chilling advances, cramps may occur in the calves, and the feet may swell. The skin, red at first, is later pale, mottled, blue or black.

Ungley and associates described three stages after rescue The prehyperemic stage lasts for a few hours to several days The extremities remain cold, somewhat swollen, discolored and numb, with fairly extensive "glove or sock" anesthesia. Peripheral arteries may be pulseless for some hours and remain so in cases going on to gangrene A hyperemic stage follows and may last from 6 to 10 weeks. In

this stage there are vascular disturbances of the skin involving temperature differentials; increase in swelling, especially if the extremities have been warmed, sensory disturbances such as tingling, usually of "glove or sock" distribution; motor disturbances; absence of sweating, and blisters, ulcers and gangrene The posthyperemic stage lasts for weeks or months after the hyperemia has subsided Except for fresh blisters or infections, the extremities are no longer unduly hot in a normal environment. In some for months or years after exposure there may be a cold-sensitive state, giving rise to the Raynaud phenomenon

Trench foot, caused by prolonged wearing of wet shoes, if cold and inaction are added factors, produces changes in the feet comparable to those observed in immersion foot

Frostbite. Cold produces vasoconstriction, and in the extremes death of tissue may result from ischemia. When ischemia is severe and prolonged, there is thrombosis of the smaller arteries which results in death of tissue and possible gangrene Freezing of the cellular fluids with crystallization and formation of ice may cause death of the tissue

In mild frostbite there is a low-grade vasculitis with panniculitis and mild inflammatory reaction In severe frostbite there is an intimitis of the smaller arteries and arterioles The endothelium of the terminal capillaries is damaged so that pathologic permeability of the capillary walls may result Thrombi are formed in the terminal arterioles

When frostbite occurs at higher temperatures and with shorter exposures than usual, and is severe, examination of the extremity often reveals thromboangiitis obliterans or arteriosclerosis obliterans

In high altitudes extremely low temperatures are encountered (—75 to —90 F) which cause an intense degree of vasoconstriction, both direct and reflex The vasoconstriction produces a marked ischemia resulting in severe anoxemia and tissue damage The anoxemia is augmented by the decreased oxygen content of the air at high altitudes.

In mild degrees of frostbite the skin of the affected region assumes a dull yellow color accompanied by numbness and a prickling, itching sensation Ice crystals may be observed in the [illegible]
exposure to cold, [illegible]
within an hour or [illegible]
tissues However, on occasion, the affected region may remain permanently hypersensitive to subsequent exposure to cold

When the deep tissues are involved by frostbite, the affected extremity is frozen stiff After thawing of the extremity, a reactive hyperemia develops. A red wheal surrounds the frozen tissue and gradually spreads over the ischemic, pale skin until the skin over the entire involved part becomes red. This phase is accompanied by tenderness, burning pain and paresthesia Blisters form and edema of the entire part often ensues. The involved tissue may become necrotic Later it may peel off and leave healed skin

In high altitude frostbite the affected part is tense and shiny and the deep tissues become dusky gray and gradually turn dark Subsequently the affected tissues shrivel and a form of dry gangrene appears

The examination reveals the extent and severity of the frostbite

In establishing the diagnosis, there is always the history of exposure to cold, and the objective signs of freezing of tissues are characteristic. The recognition of an underlying occlusive arterial disease if present is important in the prognosis of frostbite.

Hypersensitivity to Cold (Cold Allergy) Certain persons are hypersensitive to local or general contact with cold. The manifestation of this hypersensitiveness can be precipitated (1) by allergy, (2) by auto-antigens, (3) by histamine-like

substances; (4) by underlying vasomotor disturbances and (5) by disturbances in the mechanism regulating the central temperature.

Horton, Brown and Roth demonstrated that a histamine-like substance is the cause of these reactions Lewis and Love demonstrated that histamine-like substance is liberated from the skin when it is irritated by cold.

Even though the sensitivity to cold can be transferred by the intradermal injection of blood serum from a reactor to cold, the true allergic nature of this condition is largely denied.

SYMPTOMS Sensitivity to cold is a systemic as well as a local reaction Among the symptoms are urticarial lesions which develop on portions of the body exposed to cold air, particularly the face, ears, neck, hands, feet, ankles and knees. In some instances the reaction to cold may involve the mucous membranes. For instance, after cold food or cold beverages have been taken, an urticarial reaction, like angioneurotic edema, may affect a hand or a foot.

The systemic reaction is manifested by an increase of pulse rate and a decrease of blood pressure, and occasionally by syncope

Horton has expressed the belief that hypersensitiveness to cold may result in drowning, drowning could result easily before the person so affected recovered from this reaction. However, fright and inability to swim are also common causes of drowning

DIAGNOSIS. The diagnosis is made from the history. It can be confirmed by a simple cold test' A cube of ice is strapped to the forearm. In susceptible persons an urticaria-like reaction will develop.

The regular cold test as described by Hines and Brown is performed by having the patient immerse the hand and arm in water the temperature of which is from 53 6 to 57 2 F (12 to 14 C) Within 5 minutes or less an urticarial and angioneurotic edema type of reaction will occur in the parts exposed to cold. A systemic reaction is manifested by a decrease in blood pressure and an increase in pulse rate. While the test is being performed, the patient should be sitting, for syncope is likely to occur

Exposure to Extreme Cold. Reduction of heat loss in response to a cold environment is initiated by peripheral vasoconstriction If vasoconstriction is insufficient to prevent loss of heat, the body temperature falls As a response to the loss of heat, mechanisms for increased heat production are invoked These mechanisms are shivering, release of epinephrine with resultant mobilization of liver glycogen, increased metabolism of muscle tissue, increase in pulse rate, and added cardiac output Vasoconstriction of the superficial vessels reduces the environmental cooling effect by decreasing the amount of blood reaching the surface to be chilled. In effect, the body surface is permitted to remain cool while the temperature of the body interior is maintained constant as long as possible

A continued exposure to cold is accompanied with reduction of blood volume by successively withdrawing fluid, increasing the viscosity, and then withdrawing plasma protein in proportion to the fluid withdrawn, so that concentration of the protein is maintained within normal limits. Increased viscosity is maintained because of the still slower withdrawal of erythrocytes Heart failure is apparently the cause of death in severe cold exposure, and is due in part to the great increases in viscosity of the blood

The large surface area of the extremities causes them to suffer extreme degrees of decreased blood supply in order to conserve body heat. During such periods the temperature of the extremities approaches that of the environment Severe cold, however, may stimulate dilatation as a reaction to injury. Thus the vasoconstrictor response (to conserve body heat) may be abandoned for vasodilatation as a secondary, protective mechanism to save the severely cooled extremity These alterations in response will not protect the individual when the body temperature falls to 90 F

this stage there are vascular disturbances of the skin involving temperature differentials, increase in swelling, especially if the extremities have been warmed; sensory disturbances such as tingling, usually of "glove or sock" distribution; motor disturbances, absence of sweating, and blisters, ulcers and gangrene. The posthyperemic stage lasts for weeks or months after the hyperemia has subsided. Except for fresh blisters or infections, the extremities are no longer unduly hot in a normal environment. In some for months or years after exposure there may be a cold-sensitive state, giving rise to the Raynaud phenomenon

Trench foot, caused by prolonged wearing of wet shoes, if cold and inaction are added factors, produces changes in the feet comparable to those observed in immersion foot

Frostbite. Cold produces vasoconstriction, and in the extremes death of tissue may result from ischemia When ischemia is severe and prolonged, there is thrombosis of the smaller arteries which results in death of tissue and possible gangrene Freezing of the cellular fluids with crystallization and formation of ice may cause death of the tissue

In mild frostbite there is a low-grade vasculitis with panniculitis and mild inflammatory reaction In severe frostbite there is an intimitis of the smaller arteries and arterioles The endothelium of the terminal capillaries is damaged so that pathologic permeability of the capillary walls may result Thrombi are formed in the terminal arterioles

When frostbite occurs at higher temperatures and with shorter exposures than usual, and is severe, examination of the extremity often reveals thromboangiitis obliterans or arteriosclerosis obliterans

In high altitudes extremely low temperatures are encountered (−75 to −90 F) which cause an intense degree of vasoconstriction, both direct and reflex The vasoconstriction produces a marked ischemia resulting in severe anoxemia and tissue damage The anoxemia is augmented by the decreased oxygen content of the air at high altitudes

In mild degrees of frostbite the skin of the affected region assumes a dull yellow color accompanied by numbness and a prickling, itching sensation Ice crystals may be observed in the affected region If the affected member is not subjected to further exposure to cold, the appearance may become normal within a few minutes or within an hour or two and there will be no evidence of permanent damage to the tissues However, on occasion, the affected region may remain permanently hypersensitive to subsequent exposure to cold

When the deep tissues are involved by frostbite, the affected extremity is frozen stiff After thawing of the extremity, a reactive hyperemia develops A red wheal surrounds the frozen tissue and gradually spreads over the ischemic, pale skin until the skin over the entire involved part becomes red This phase is accompanied by tenderness, burning pain and paresthesia Blisters form and edema of the entire part often ensues The involved tissue may become necrotic Later it may peel off and leave healed skin

In high altitude frostbite the affected part is tense and shiny and the deep tissues become dusky gray and gradually turn dark Subsequently the affected tissues shrivel and a form of dry gangrene appears

The examination reveals the extent and severity of the frostbite

In establishing the diagnosis, there is always the history of exposure to cold, and the objective signs of freezing of tissues are characteristic. The recognition of an underlying occlusive arterial disease if present is important in the prognosis of frostbite.

Hypersensitivity to Cold (Cold Allergy). Certain persons are hypersensitive to local or general contact with cold The manifestation of this hypersensitiveness can be precipitated (1) by allergy, (2) by auto-antigens; (3) by histamine-like

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or even to temperatures near 90 F, a fact which is made evident by cold injuries occurring at a body temperature of 95 F. A decrease in the temperature of the interior part of the body may be produced by any prolonged exposure when an excess of heat loss over heat production is operative. For instance, a prolonged immersion of the body in cold water, when the rate of heat loss is twenty times as great as in air, results in depression of body temperature. Molnar has asserted that an exposure of 1 hour in water at 40 F can be expected to kill one half of the persons thus exposed. The more rapid heat loss in water is due to the poorer insulative value and the higher conductivity of water

Hypothermia occurs from exposure to cold air when the body is not protected by adequate clothing Despite proper clothing, children, old and cachectic persons, exhausted persons, and all persons during sleep, undergo heat loss because the efficiency of the temperature regulatory mechanism is reduced Hypothermia is likely to occur if those whose clothing is wet with water are forced to remain exposed to the cold and to a strong wind

In extreme hypothermia often the patient is not seen by the physician until a deathlike state is present In any instance of a deathlike state after exposure to cold, if rigidity of the muscles is absent, the diagnosis of hypothermia is a good probability. There is hope for recovery if proper treatment is administered; therapy for acidosis is very important

In many instances prolonged hypothermia leaves the heart permanently dilated Psychic derangements such as hallucinations and apoplectiform and epileptiform states may ensue as permanent after-effects of a prolonged hypothermic experience.

Cold Injury and Death. Deaths from cold introduce an element of acidosis and shock. The effect of freezing a part of the body is to fix the fluids solid, both in the vessels and in the tissue spaces Life is suspended, and whether it can be resumed again depends entirely on the ability of the tissues involved to survive the complete anoxia which has taken place.

When cold pervades the body, metabolism is lowered and the body temperature may fall to a level at which vital processes cease Death is preceded by a sense of fatigue and drowsiness, and the victim may fall into a confused sleeping state which obscures the bitterness of cold and exposure

Necrospy provides little evidence of these functional changes except where they are localized, as in immersion foot. The outstanding features are capillary dilatation and increased permeability resulting in edema of the tissues. Blebs may develop in the skin Clumped aggregations of erythrocytes are sometimes seen in parts killed by freezing

An interesting phenomenon may occur when freezing has preceded the development of rigor mortis. The muscles may soften as they thaw, and then rigor mortis may pursue its ordinary course

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mediate clinical importance. The important feature is the loss of electrolytes (sodium, chloride, potassium) and water The chronic diarrheal states which may cause loss of electrolytes in sufficient amounts to cause symptoms of electrolyte loss of a sufficient degree to be immediately important are pellagra and sprue. In these there is an inadequate diet or inadequate absorption (sprue). An inadequate absorption also may result from loss of sufficient intestinal surface for absorption and this may follow surgical removal or surgical anastomosis in which a long segment of the intestine is left in a malfunctioning state

Diseases of the urinary and genital organs or endocrine glands are not important causes of nutritional deficiency disease if diabetes mellitus or hypothyroidism is discovered and treated Likewise diseases of the nervous system or organs of special senses rarely are complicated by diseases secondary to metabolism. Loss of taste and smell in patients who are not mentally deranged will not greatly interfere with eating Loss of appetite in the insane requires special care not within the scope of this consideration

There are a number of conditions which may cause an increased requirement of food Important among these is increased physical activity, voluntarily or involuntarily imposed In the latter group of conditions is the physical exertion accompanying delirium, convulsive states (status epilepticus) and maniacal states. Pregnancy, lactation, hyperthyroidism and excessive perspiration require increased amounts of food

There are many drugs which interfere with appetite sufficiently to cause deficiency disease or other metabolic disturbances Fortunately, however, only the physicians who are therapeutic enthusiasts continue administration of such drugs long enough to cause serious trouble. Chronic alcoholics and drug addicts frequently develop deficiency diseases

DISEASES DUE TO DEPRIVATION OF VITAMINS

Vitamin A. Vitamin A is a fat-soluble vitamin formed in the liver from the carotenes, and stored in this organ It is a constituent of visual purple (rhodopsin), preserves the integrity of epithelium, and influences calcium metabolism. It is synergistic to the sex hormones and cortin but antagonistic to the thyroid gland and insulin

The minimal daily requirements are 1,500 I U (international units) for infants, 3,000 for children up to 12 years of age, and 5,000 for older children and adults An excess of vitamin A due to overdosage may produce toxic manifestations but this is rare

Hypervitaminosis A. Hypervitaminosis A is reported to occur in the children of parents who are extremely concerned about adequate vitamin administration, and in each instance there is a history of excessive dosage with vitamin concentrates

The storage of vitamin A and the regulation of its blood level are functions of the liver Because of the capacity of the liver to store enormous amounts of the vitamin, Fried and Grand have expressed the belief that the syndrome is caused by hepatic dysfunction rather than by supersaturation of the liver with the vitamin Curves for vitamin A absorption demonstrate the existence of hepatic dysfunction

The predominant symptoms are anorexia, irritability, generalized pruritus and painful extremities, with a reluctance to stand or walk

There is a uniform similarity in physical observations, for all these patients have a yellowish pallor, sparse coarse hair, dry scaly lips with bleeding fissures at the corners of the mouth, and dry excoriated skin, hepatomegaly, tenderness over the long bones, and generalized weakness.

Roentgenologic examination reveals irregularities in cortical structure of the bones such as periosteal elevation with a single layer of subperiosteal new bone

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DISEASES DUE TO OR ASSOCIATED WITH DISORDERS OF METABOLISM

Metabolism may be considered as all of the physical and chemical processes by which living organized substance is produced and maintained. Diseases due to or associated with disorders of metabolism may be due to lack of food In such instances the ensuing disease is primary starvation. In contrast to primary starvation are those conditions which arise from an inadequate diet and are termed secondary nutritional deficiencies Secondary nutritional deficiency diseases accompany various environmental conditions and bodily states. These may be listed as follows (1) increased food requirements; (2) interference with the ingestion of food; (3) interference with the absorption of the chyme; (4) failure of utilization after absorption; (5) increased excretion of metabolic products, and (6) increased or interrupted destruction of metabolic products

The secondary nutritional deficiencies most frequently follow prolonged inability to partake of a sufficient amount of foods The ingestion of food is limited by a loss of appetite The three commonest conditions initiating loss of appetite are fever, pain and anorexia nervosa Fevers accompany all active generalized infections, certain allergic or chronic anaphylactic states such as rheumatic fever and rheumatoid arthritis, generalized malignant lesions and some of the chronic blood dyscrasias These diseases comprise a large part of all human illnesses

Pain from any cause, particularly if situated about the head, face, neck or abdomen, is very apt to blunt the appetite If pain is severe or of moderately long duration the administration of opiates and sedatives may add to the difficulty of eating

Anorexia nervosa may not be easily detected. Many patients vow that they ingest large amounts of food These assertions are often found not to square with the facts after the alimentary tract has been examined and found to be free of disease.

A systemic review of the causes of the development of nutritional deficiencies reveals that aside from pain, diseases of the locomotor system which interfere with the ingestion of a proper amount of food are referable to ankylosis of the temporomandibular joint and conditions of extreme weakness of the muscles such as occur in myasthenia gravis and in the muscular dystrophies

There are no respiratory diseases which prevent eating except those affecting the pharynx and those creating extreme dyspnea Likewise dyspnea from cardiac disease may prevent eating. Dyspnea may accompany severe anemia from a blood [illegible]

[illegible] sec-

[illegible] tract

[illegible] consisting of narrowed segments occurring anywhere from the esophagus to the anus may cause starvation by degrees as the child grows and requires more foods than are supplied by milk formulas. Of these congenital malformations, congenital hypertrophic pyloric stenosis is common and occurs early in life Acute infections, food poisoning or irritations cause acute gastroenterocolitis accompanied by vomiting and diarrhea. In these acute conditions and in pyloric and intestinal obstruction, it is not the lack of food or the development of a nutritional deficiency that is of im-

It is well to remember that the response of cutaneous lesions to vitamin A, even if the lesions are due to vitamin A deficiency, is slow in contrast to the relief of night blindness in which the response depends on physiologic changes Night blindness is promptly relieved by administration of vitamin A

Vitamin A and Diseases of the Skin. A secondary deficiency of vitamin A has been postulated to have some significance in a few rare cutaneous diseases, for instance, Darier's disease, pityriasis rubra pilaris and ichthyosis. However, in these as well as the vast majority of cutaneous diseases there is little or no direct relationship

If large amounts of vegetables containing carotene are ingested by normal persons and persons suffering from certain diseases such as diabetes, carotene may accumulate in the skin in amounts sufficient to cause a deep yellow color This condition is known as *carotenemia* This skin coloring, so far as is known, is important only from the undesirable aspects of the cutaneous discoloration. Patients who have this discoloration may have false positive icterus index readings

Vitamin B Complex. Vitamin B complex includes a number of well-defined substances All of them are closely associated in nature, are widely distributed in natural foodstuffs, and are water soluble

Thiamine Hydrochloride (B_1). Vitamin B_1 has been synthesized and identified as thiamine hydrochloride. In foodstuffs and in the body vitamin B_1 combines with pyrophosphoric acid and functions as a cocarboxylase, an enzyme which has an important role in the metabolism (oxidation) of pyruvic acid It acts as a catalyst coenzyme in the metabolism of carbohydrate, promotes appetite and the growth of children, and is necessary for proper nerve function The daily maintenance requirement is thought to be about 0.5 to 1 0 mg in children, 1.5 to 2.0 mg in men and women.

Since a deficiency of thiamine results in an increase of pyruvic acid, blood tests are based on quantitative determinations of the latter. Pyruvic acid is stated to vary normally from 3 7 to 5 8 mg per 100 ml of blood with an average of 4 7 mg

Death has occurred immediately after the intravenous injection of thiamine hydrochloride The untoward reactions are in the nature of hypersensitivity to the vitamin

Beriberi. Beriberi in the adult is classified as (1) dry beriberi when degeneration of the nervous system, chiefly a multiple peripheral neuritis, is the outstanding manifestation, (2) wet beriberi when serous effusions and edema are the outstanding features, (3) fulminating beriberi when acute in onset and manifested by acute cardiovascular symptoms A combination of two or more of these types is referred to as mixed beriberi and this form is commonly observed

In acute beriberi the heart is dilated and enlarged In Oriental beriberi the enlargement is most pronounced in the right side of the heart where the muscle is coarse and firm and papillary muscles are especially prominent The valves are normal Degeneration of medullary and myelin sheaths and ganglion cells has been observed.

Symptoms The symptoms of beriberi commence with loss of weight, strength and appetite which precede the neuritis Difficulties in concentration, attention and comprehension, and memory defects too may commence before any evidence of peripheral neuritis

There is an ascending symmetric, peripheral neuritis, of which the initial symptoms are pain, weakness and cramps in the legs. There may be burning and numbness of the ankles and feet and impairment of dorsiflexion of the toes.

Involvement of the phrenic nerve or of the recurrent laryngeal nerve may occur. The sphincter muscles are affected in the late stages of the disease There may be ataxia and in-co-ordination. Contractures are common when paralysis is of long standing

The cardiac symptoms of beriberi are those of congestive failure. There are dyspnea and palpitation on exertion, tachycardia and edema. Acute heart failure

along the midportions of the shafts of the ulna, the clavicle, femur and tibia. There is a significant increase in the concentration of the blood vitamin A above the accepted normal value (50 to 300 I.U. per 100 ml. of plasma).

Vitamin A Deficiency. A deficiency of vitamin A may produce (1) keratinization of epithelium resulting in xerophthalmia, keratomalacia and follicular keratosis of the skin; (2) night blindness or nyctalopia; (3) osseous metaplasia; (4) the formation of renal calculi and, possibly, (5) prolongation of the period of gestation.

Hyperthyroidism may deplete or destroy vitamin A reserves. It seems that the thyroid hormone may participate in the conversion and storage of vitamin A, and thus vitamin A may be destroyed more rapidly when the metabolic rate is increased from any cause

The clinical observation is said to indicate that night blindness and keratomalacia may attend disease of the liver. Patients who have a slowly progressive cirrhosis of the liver may have subnormal powers of adaptation of their vision to darkness This aberration of vision improves on adequate administration of vitamin A.

SYMPTOMS. Most of the symptoms of vitamin A deficiency, except when the disease occurs in epidemics, are not separable from those of commoner diseases. In sporadic cases, therefore, the symptomatology is of little importance in the diagnosis

The loss of visual acuity in dim light is one of the first symptoms of vitamin A deficiency in man. Xerophthalmia is commonest in infancy although it may occur at any age. Night blindness develops in adults before any ophthalmias develop.

EXAMINATION Dryness and scaliness of the skin are early observations in those who have a deficiency of vitamin A One type of cutaneous lesion is characterized by small pustules which appear around the hair follicles on the extensor surfaces of both upper and lower extremities, on the shoulders, on the lower part of the abdomen and on the buttock These pustules vary in diameter up to 5 mm, are hard and deeply pigmented, and have a surrounding area of depigmentation. In the center of each pustule is an epithelial plug which when expressed leaves a crater

In the early stages of the disease the ophthalmologist observes small triangular white areas on the outer and inner sides of the cornea covered by white spots consisting of corneal epithelium which has been shed and has accumulated in this position (Bitot's spots) Photophobia and conjunctivitis appear early, followed by a light brown pigmentation of the conjunctiva. The keratinization of the conjunctiva may extend to the cornea and lead to extreme softness and degeneration of the cornea and to ulceration, perforation and total destruction of the eye (keratomalacia). This disease may destroy the eye rapidly

Vernix caseosa is a manifestation of a vitamin A deficiency in the newborn infant and it represents disturbances in cornification analogous to the dermal changes accompanying keratomalacia and other manifestations of vitamin A deficiency

In the infant, keratinizing metaplasia may appear in the trachea, bronchi, in the renal pelves, in the conjunctivae, corneas, accessory sinuses, salivary glands, ureters, uterus and periurethral glands

DIAGNOSIS. The incidence of vitamin A deficiency in the United States is low and therefore the likelihood of necessity for diagnosis is small. Vitamin A deficiencies are best detected by biophotometric examinations of the eyes There is relation between the biophotometer reading and vitamin A nutrition, but this relation is not definite enough to use as a means of diagnosing subclinical vitamin A deficiency. The small quantities of vitamin A present in the blood stream of man cannot be accurately determined by present methods

If there are cirrhosis of the liver, hyperthyroidism, prolonged pyloric obstruction, severe chronic diarrhea, or a generalized nutritional deficiency from any cause, vitamin A deficiency is a likely diagnosis.

yellowish crust which forms at the angles may be removed without bleeding. If the lesions recur frequently, a cicatrix may be formed, giving the affected area an atrophic appearance. The tongue is reddened and congested.

Often there is conjunctivitis. The eyes itch and burn and there is photophobia, which is often a manifestation of a superficial keratitis. Interstitial infiltration with exudation often gives rise to opacities either punctate or generalized. In some cases there is also involvement of the iris. The ophthalmologist is greatly aided in these examinations by employment of the slit lamp.

On the skin there is often a fine, scaly desquamation on a mildly erythematous base This desquamation may be present on the alae nasi, within the nostrils, and on and about the ears.

DIAGNOSIS The diagnosis of riboflavin deficiency depends on the presence of stomatitis and cheilosis, conjunctivitis and growth of the conjunctival vessels into the cornea, and seborrheic changes in the skin of the face, particularly of the nose and adjacent regions.

Nicotinic Acid. Nicotinic acid or niacin is highly effective in the prevention of pellagra, niacin and nicotinamide together are known as the P.P. (pellagra-preventing) vitamin Nicotinic acid is prepared synthetically

The normal maintenance dose of nicotinic acid has been estimated as varying from 17 5 to 35 mg per day The mean level for whole blood is 438 micrograms per 100 ml The normal range lies within the limits 260 to 573 micrograms per 100 ml of blood (Carter and O'Brien) The blood concentration of nicotinic acid is constant over a period of time but is temporarily increased after the administration of large doses of nicotinamide

Pellagra Pellagra follows a prolonged dietary inadequacy of nicotinic acid and substances physiologically similar The disease is particularly prevalent among the poor and ignorant who are forced to live on an unbalanced diet, usually rich in carbohydrates and fats but low in proteins, minerals and vitamins It occurs too in the ignorant well-to-do who by choice live on this same sort of diet. In these two groups of cases the disease is called endemic pellagra.

Alcohol addicts often subsist mainly on calories derived from alcohol, thus pellagra develops which is termed alcoholic pellagra or pseudopellagra.

[illegible] ave lost

[illegible] disorder attributed to respiratory enzyme systems, coenzymes I and II, occurs In the presence of such a disturbance there arise functional disturbances such as vasomotor instability in the skin, and disorders of alimentation, the nervous system, and the circulatory system The most readily affected systems seem to be those weakened by hereditary predisposition or trauma

SYMPTOMS [illegible]

General muscula [illegible]

of memory, head [illegible]

sations in various parts of the body, vertigo, numbness, nervousness, palpitation, distractability, flights of ideas, apprehension, morbid fears, mental confusion and forgetfulness frequently are present There may be alternating diarrhea and constipation These symptoms are so commonly observed in the neurotic patient that it may be difficult to recognize that they constitute a syndrome of a serious disease.

The clinical symptoms of endemic pellagra may develop in infants and children in pellagra families The distinctions between the symptoms of infant pellagrins and those of adult pellagrins can be made when it is realized that in the adult patient deficiencies affect mature tissues, whereas in the infant or child the rapidly growing tissues are more susceptible to injury than in the adult person

EXAMINATION On examination the cutaneous lesions may appear symmetrically placed They are most frequently observed on the flexor surfaces of the hands, wrists

may occur abruptly, with paroxysmal dyspnea, cyanosis, increased venous pressure, tachycardia, precordial pain and a small thready pulse.

EXAMINATION. The Achilles and patellar reflexes may be diminished and finally absent The weakness in the legs extends proximally, producing toe drop and drop foot. The muscles of the arms usually are not affected, until the symptoms of the lower extremities have become severe

[illegible] il parts of the legs. Appreciation of vibra- [illegible] is present in the lower extremities in a [illegible] by anesthesia.

Atrophy of the muscles of the legs is common. However, the degree of atrophy may be obscured by the presence of edema

Affections of the vagi nerves outside of the cranium may cause difficulty in swallowing and regurgitation There may be vocal disturbances, stridor and dyspnea among many other symptoms, depending on the extent of involvement of various cranial and peripheral nerves

In uncomplicated beriberi the arterial blood pressure is usually normal or low, often with an increased pulse pressure. The venous pressure is generally increased but may be normal Electrocardiographic changes, chiefly of the T wave and QT interval, have been observed

During failure the heart is enlarged, with associated pulmonary congestion The speed of circulation is increased in the cardiovascular type of beriberi, whereas in other congestive failure, except that due to hyperthyroidism, there is usually a conspicuous slowing of the circulation Hydropericardium, hydrothorax and ascites may be present as the result of the primary disease or of heart failure.

DIAGNOSIS Beriberi is a primary deficiency disease In the United States beriberi is associated with functional and organic gastrointestinal diseases, chronic debilitating diseases, pernicious vomiting of pregnancy, chronic alcoholic addiction, diabetes, pellagra, rapid growth, pregnancy, lactation, febrile illness, and hyperthyroidism.

The diagnosis of beriberi is based on the history, the symptoms and the physical findings, for there is no satisfactory diagnostic test for thiamine deficiency The response to an adequately controlled therapeutic test is pathognomonic of thiamine deficiency

Thiamine Deficiency and Hyperthyroidism. Increased requirements for essential factors tend to produce a relative deficiency of thiamine. This relative deficiency of thiamine contributes to the symptomatology of hyperthyroidism. Manifestations which are commonly present in both hyperthyroidism and thiamine deficiency are diarrhea, tachycardia, enlargement of the heart, dyspnea, palpitation, edema, fatigue, loss of muscular strength, neuritis and disturbances in carbohydrate metabolism

Riboflavin (B_2). Riboflavin or vitamin B_2 is also known as vitamin G. It occurs as a fluorescent pigment widely distributed in plant and animal tissues Yeast and liver are its richest sources The minimal requirement for adults has been estimated at 2.2 to 2.7 or about 3 mg. per day

The absence of riboflavin in the urine is indicative of its deficiency According to the method of Strong, in the normal person about 480 to 800 micrograms are excreted in the urine in 24 hours.

Riboflavin Deficiency. Riboflavin deficiency is commoner in women than in men The incidence tends to be higher in the spring and summer than at other seasons of the year. Persons who have other deficiency diseases are likely to have riboflavin deficiency too

SYMPTOMS It is impossible to separate the early symptoms of spontaneous riboflavin deficiency from those of pellagra or beriberi.

EXAMINATION. On examination in the early stages of riboflavin deficiency there may be paleness of the lips, particularly at the angles between the lips. Superficial fissures usually are present at the corners of the mouth The lesions are dry, and a

Subperiosteal hemorrhages are common, and may be confined to the ends of the shaft where the periosteum is separated easily from the bone In advanced stages of rickets the entire length of the periosteum may be separated from the bone

The dentin in adults is resorbed. The pulp reveals atrophy, hyperemia and degeneration. Rarefaction of the alveolar bone results in loosening of the teeth

The skin over the trunk and lower extremities commonly contains perifollicular petechiae. Ecchymoses are commoner about the knees and ankles. Moderate effusions, often blood-tinged, may occur in the pericardial, pleural and peritoneal cavities. Hemorrhage may be found anywhere in the body.

In adult scurvy there occurs fragmentation of the fibers of striated muscles which later become replaced by connective tissue

Infantile Scurvy. [illegible] infants, it develops in some brea[illegible] ages of 8 and 13 months, are n[illegible] as loss of appetite, irregular diarrhea, and failure to gain weight There are associated pallor, apathy, irritability and increased susceptibility to infection. The infant is small for the age and cries when approached

Fever and increased pulse and respiratory rates are common in infants who have manifest scurvy Rapid, shallow breathing, out of proportion to the fever and pulse rate, may be due to painfulness of the ribs and costochondral junctions. Epistaxis, vomiting of blood, and bloody stools may be the chief complaint Hemorrhage may occur in the abdominal organs Orbital hemorrhage may cause proptosis Ecchymoses of the eyelids are common and may be associated with edema Subconjunctival hemorrhage is rare; the eyeballs usually are not affected Hemorrhage into the brain or meninges may cause symptoms of intracranial hypertension

On examination the findings are essentially the same as in adult scurvy

Adult Scurvy. A prolonged period of deprivation of ascorbic acid (vitamin C) is required to produce adult scurvy. There is a great variation in the susceptibility of different persons to scurvy which was first definitely proved among the personnel of ships long at sea

The symptoms may begin with aching pains in the muscles of the calves, and painful swelling of the knees and edema of the ankles.

The gums become swollen and hemorrhagic Hemorrhages in the muscles cause brawny induration and tenderness Petechiae and ecchymoses occur in the skin. Epistaxis, and hemorrhages, conjunctival, retinal, cerebral, gastrointestinal, and urogenital, are rare in adult scurvy

On examination the findings in the infantile and adult forms of scurvy are essentially the same except that they are severer in the infantile form There is loss of weight if there is no edema The tissues are soft and muscle tone is decreased The complexion is pallid and often there are edema of the face and swelling of the pinnae of the ears and of the scalp

The gums appear swollen, congested and dark red or purple In some instances the teeth are buried by the swelling Hemorrhages are present, and additional hemorrhages occur readily on slight trauma to the gums.

Petechiae and ecchymoses of varying sizes are commonest in the lower extremities, in the lower half of the trunk, and in the forearms, face and neck. Miliaria, if present, is not specific for scurvy The tourniquet test is positive

Swelling of the extremities, due to subperiosteal hemorrhage, is commonly present It appears suddenly after mild trauma Pain and tenderness may be localized at the swelling or may extend over the entire extremity. There is a series of tender nodules at the costochondral junctions. In extreme instances the sternochondral plate is displaced posteriorly. Submetaphysial infractions (epiphysial separations) are commonly revealed by roentgenologic examination.

[illegible] on finding. In [illegible] The number [illegible] ually normal,

and feet. The skin over the elbows, knees, face and neck and under the breasts and in the perineal region may be affected. In most instances the area of dermatitis is sharply demarcated from the normal skin In some who have pellagra the cutaneous lesions are absent and this condition has been termed pellagra sine pellagra. The mucous membranes of the tongue, the oral cavity and the vagina may reveal glossitis, stomatitis and vaginitis as early manifestations of the disease

As the disease advances, there are loss of memory, excitement, mania, delirium, and hallucinations, and finally dementia.

DIAGNOSIS. The diagnosis of pellagra is based on the appearance of the cutaneous lesions Lesions of the skin associated with diarrhea and aberrations of the central nervous system affecting both the psyche and the soma are often pellagral in origin. Response to treatment in some cases has to be resorted to for purposes of diagnosis.

Other Members of the Vitamin B Complex. The substances enumerated in the following paragraphs are part of the vitamin B complex. From time to time they have been considered of significance in nutrition, but thus far their role has not been well defined, nor have the daily requirements for human beings been established

Pyridoxine or vitamin B_6 occurs in unrefined cereals, legumes, fish and meats

Pantothenic acid occurs naturally in milk and various vegetables and is prepared synthetically. It can be determined in the whole blood and is stated to vary normally from 0 019 to 0 32 microgram per cubic centimeter

Vitamin B complex includes *biotin or vitamin H, the role of which in human nutrition* is as yet unknown

Animal investigations have indicated that along with pantothenic acid and biotin *para-aminobenzoic acid* may regulate the pigmentation of hair and affect the formation of melanin There appears to be no justification at present, however, for its use in the treatment of premature graying of human beings

Inositol probably influences the growth and maintenance of hair although its value in this connection in human beings is not known

Choline, like nicotine, causes a preliminary stimulation and finally a paralysis of the autonomic ganglia, resulting in a marked drop in blood pressure, increased peristalsis and a general increase in the secretions

Folic Acid and Vitamin B_{12}. Folic acid (pteroylglutamic acid) is the synthetic Lactobacillus casei factor. It occurs naturally in the liver, kidneys and other animal tissues; likewise in yeast, mushrooms, grass and green leaves Vitamin B_{12} is of unknown chemical structure

Microscopic examinations of the blood are the only means of identification of the particular macrocytic anemias in which the compounds have been found of therapeutic value The diagnosis is confirmed if the anemia improves on administration of the vitamin

Vitamin C (Ascorbic Acid). Vitamin C occurs naturally in citrus fruits and in vegetables It is destroyed by exposure to air, alkali and heat Tomato juice, because of its high acidity, can be canned without much loss Most fruit juices can be concentrated in vacuo or by the spray process without appreciable loss of the vitamin.

Vitamin C is cevitamic or ascorbic acid and is prepared synthetically Its unique action in the body is largely due to reducing properties promoting oxidative or respiratory mechanisms in the tissues It maintains capillary resistance and affects the functioning of odontoblasts in the formation of dentin It is synergistic to cortin and insulin The daily maintenance requirements for infants are 10 mg, about 15 to 20 mg for children more than 1 year but less than 12 years of age, and about 30 mg for adults.

Normally from 0.7 to 1.4 mg of ascorbic acid (vitamin C) occurs in 100 ml of blood plasma under fasting conditions, the amount varying with the intake.

The defective osteoid formation is most pronounced in the distal end of the femur, the proximal end of the humerus, both ends of the tibia and the fibula, and the distal end of the radius.

Normal marrow at the epiphysial ends of the bone is replaced by soft fibrous tissue.

woman may have children who become rickety by a man who has had rickets, and she may have healthy children by another man who has not been rickety. The sexes are equally affected

SYMPTOMS. The baby cries abnormally on being handled, particularly when the ankles are handled in changing the diaper. The infant makes no attempt to move the legs or (sometimes) the arms Often the voluntary movements consist solely of tossing the head from side to side while crying

The disease usually is fully developed by the end of the second year of life, and then quickly recedes. However, there are instances of "late" rickets In late rickets the most active stage of the disease is observed in the third or fourth year of life or recurs at the time of puberty In the late forms, coxa vara with high position of the trochanter, shortening of the leg, with limitation of abduction, atrophy of the muscles of the gluteal and femoral regions, genu valgum, flatfoot and spinal curvature are common. Before condemning the pediatrician who has been in charge, it is well for the diagnostician to inquire about the dieting program that an adolescent has been on, because this disorder often is encountered despite good dietary habits and good food.

During the course of infantile rickets tetany may develop.

EXAMINATION Tenderness of the extremities and pain on movement due to hemorrhage are apparent on examination Hemorrhages occur most frequently under the periosteum of the long bones, in the gums, the skin and the mucous membranes, and at the lower end of the femur followed by bleeding in the upper end of the humerus Hemorrhage occurs much less frequently at the ankles and the wrist The hemorrhage under the periosteum may be so great that swelling of the bone may be evident The periosteum of long bones fuses with the perichondrium near the ends and therefore the swelling does not extend beyond the end of the bone or involve the joint The bone thus becomes club-shaped

Changes in the *skull* are often the first to be evident on examination. The bones of the skull are thin and soft The occipital bones may be so soft that they can be dented with the finger tip (craniotabes) On pressure with a finger over such areas parchment-crackling may be present.

The forehead and parietal bosses become prominent from thickening of the frontal and parietal bones. The resulting square forehead formed by prominent frontal eminences resembles in appearance the hydrocephalous cranium.

Dentition is delayed, and the teeth, when they do appear, are small (microdontia) and deformed.

The rachitic rosary, in the *thorax,* arises from thickening at the costochondral junction of the ribs with their cartilages. When well advanced, these enlargements can be palpated Excessive softening of the ribs leads to distortions and deformities of shape of the thorax These deformities consist of outward curving of the margin of the lower aperture of the thorax, vertical grooves on each side of the sternum; horizontal groove at the level of the xiphoid, producing *Harrison's groove;* pectus carinatum or pigeon breast. Kyphosis or kyphoscoliosis are commonly caused by rickets Diminution of the pubosacral diameter and other pelvic deformities in girls may complicate childbearing

The increase in size of the epiphyses proximal to the wrist and ankle are characteristic The long bones of the forearms and of the legs are soft and become curved, producing bowlegs and knock knees. A mild grade of rickets predisposes to frequent greenstick fractures

In rickets the muscles are loose and poorly developed, so that a greater freedom of joint movements is possible than in normal persons These rachitic patients are double-jointed

In adults misshapen heads, bowlegs, thoracic deformities, and, in the female, narrow pelves are often the residua of infantile rickets.

but in severe scurvy prolongation of either or both may occur There may be changes in the values for the serum calcium and inorganic phosphorus, but these changes are not constant. Hematuria occurs with great frequency; oliguria is common Hyaline or granular casts, sometimes blood casts, and pyuria may be present

Characteristic roentgenologic changes in the bones are most helpful diagnostically. A positive reaction to capillary resistance tests and a decreased blood level (normal range 0 7 to 1 4 mg) of ascorbic acid suggest a depletion of vitamin C.

A history which reveals evidence of inadequate intake of foods containing vitamin C is helpful diagnostically If the diagnosis remains in doubt, a therapeutic test is recommended 250 mg. of ascorbic acid should be given parenterally each day The patient is observed for alteration of symptoms and if the symptoms disappear, the diagnosis is established.

Vitamin D. Vitamin D is fat soluble and occurs naturally in fish liver oils as well as in egg yolk, liver, butter and salmon It is produced in the body on exposure to sunlight

At least 10 sterol compounds possess vitamin D activity Two of these, D_2 (calciferol), produced by the irradiation of ergosterol, and D_3, formed by the irradiation of 7-dehydrocholesterol, a precursor of vitamin D present in the outer layers of the skin, are of known importance

Vitamin D is not absorbed from the intestinal tract in the absence of bile Its chief function appears to be concerned with the metabolism of calcium and phosphorus The characteristic changes in deficiency are (1) diminished serum inorganic phosphorus, (2) usually a diminished serum calcium, (3) increased serum phosphatase activity, and (4) a negative calcium and phosphorus balance with excessive elimination of these elements in the feces

The minimal daily requirements of vitamin D are 400 U S.P. units, irrespective of age A deficiency in vitamin D may result in rickets, consequently it is called the antirachitic vitamin

There are no laboratory examinations available for the detection or estimation of vitamin D in the blood or the urine

The concentration of phosphate in the blood is greater in the summer than in the winter The concentration of inorganic phosphate, in rickets, is more constantly lowered than is that of calcium The product of concentrations of calcium and phosphorus is usually in the region of 40 but falls below 30 in the great majority of rachitic infants.

Vitamin D increases the serum phosphate by increasing the intestinal absorption of calcium or by diminishing its re-excretion from the intestinal mucosa Parathyroid extract increases the concentration of serum calcium by withdrawing the element from the bone

Rickets (*Rachitis*) The inheritable rate of growth is a most important predisposing factor in the production of infantile rickets Slow growth encourages the onset of rickets

Breast milk in sufficient quantities largely prevents rickets Metabolized milk and irradiated milk possess antirachitic activity about equal to that of human milk but are of value only in prevention and should not be depended on in treatment of active rickets

During the development of rickets the epiphysial cartilage increases irregularly in width. The basic structural alteration in rickets is not the failure of formation of bone but the failure of calcification

The lower epiphysis of the femur most commonly will reveal a wide, irregular zone of ossification at the junction of the epiphysis and the diaphysis This region is known as the rachitic zone. Growth of the bone is delayed or stopped completely, in proportion to the severity of the process The structural changes in the bone are not identical in all instances. In one type of the disease there is a large medullary cavity with a thin, porous cortex; in another type the cortex is thick but porous and the medullary cavity is small

Rickets is rare in the tropics, at high altitudes, and in northerly regions, though it does occur in any climate provided there is the proper hereditary background A

subcutaneous tissues. Periarticular calcification also has been described in man which may clear up on cessation of the administration of the vitamin.

The mechanism of the disorder is not entirely clear. The manifestations are probably associated with one or both of the known actions of vitamin D: (1) to increase calcium absorption from the gastrointestinal tract and (2) to increase phosphorus excretion in the urine.

The symptoms include anorexia, lethargy and constipation, polyuria and polydipsia.

There are no essential physical findings. There are present albuminuria, hyposthenuria, impaired renal function, hypercalcemia and hyperphosphatemia or hypophosphatemia.

Essential in making the diagnosis is the history of excessive administration of vitamin D and the presence of the afore-mentioned calcifications.

The maintenance dose in human beings is unknown.

Vitamin K. Vitamin K occurs naturally in alfalfa, cabbage, spinach and cauliflower. It is produced synthetically in a form known as K_1 or 2-methyl-3-phytyl-1, 4-naphthoquinone, and as K_2 In man, under normal conditions, the minimal requirements for vitamin K seem to be produced by bacteria in the ileum and the colon Since natural vitamin K is oil-soluble, its absorption cannot occur unless normal amounts of bile are present.

Coagulation of the blood proceeds normally if sufficient amounts of fibrinogen and thrombin are present to produce fibrin Thrombin is formed only from its precursor prothrombin Prothrombin is produced in the liver, provided vitamin K is available. Intravascular coagulation is prevented by antiprothrombin (presumably heparin). In the event of a wound, thrombokinase is liberated by the platelets and tissues and mobilizes thromboplastin The latter fixes antithrombin, and the free prothrombin is then activated by the calcium salts of the blood with the production of thrombin

A deficiency of vitamin K results in hypoprothrombinemia and this, in turn, in prolonged bleeding However, hypoprothrombinemia may be caused (1) by a lack of vitamin K due to temporary sterility of the intestinal tract, (2) by inadequate absorption of vitamin K due to insufficient bile in the intestine, as in biliary and gastrointestinal fistula, obstructive jaundice and intestinal obstruction, or because of impairment in its absorption as in ulcerative colitis and sprue, (3) by imperfect utilization of vitamin K by the liver in the formation of prothrombin due to primary hepatic disease, as in cirrhosis, hepatitis, and acute yellow atrophy, or (4) by surgical removal of long segments of the small intestines.

There are no direct laboratory examinations for the detection of vitamin K deficiency in the blood or urine Several tests are available, however, for determining the prothrombin content of the plasma, for example, that of Quick. By the Quick method plasma normally produces coagulation in 19 to 20 seconds. There is a wide margin of safety, for when prothrombin is reduced in the plasma to between 30 to 40 per cent of normal the prothrombin time is usually at the upper limits of normal or about 20 seconds, when reduced to about 10 per cent of normal, it is likely to be around 40 seconds, and when reduced to 5 per cent, around 70 seconds.

A determination of the prothrombin concentration of the blood may be a reliable index of hepatic function, provided the intake of vitamin K is adequate.

PHYSICAL FINDINGS OF VITAMIN DEPRIVATION

In the preceding paragraphs the diagnosis of nutritional deficiency diseases has been based largely on the presence of certain physical findings such as conjunctival thickening, corneal vascularization, hyperkeratosis, cheilosis, glossitis, swollen and bleeding gums, petechial hemorrhages and neurologic manifestations. In a recent review, Darby pointed out the fallacy of relying on such physical findings only and cited a number of diagnostic errors that have arisen from lack of experience and judgment of those who make such medical appraisals A thicken-

DIAGNOSIS The diagnosis can be made and often is made on the basis of physical findings alone After the disease has developed, or perhaps after it has healed, roentgenographic evidence is often diagnostic.

Rickets may resemble infantile scurvy, purpura simplex, congenital syphilis, chondrodystrophy, osteogenesis imperfecta, cretinism, congenital dislocation of the hip and hydrocephalus.

Osteomalacia (*Adult Rickets*). The term osteomalacia is used to designate the existence of a skeletal disease characterized by bone softness. It is generally agreed that osteomalacia and infantile rickets are the same disease (see Diseases of the Bones, Chapter 6) In the adult who has osteomalacia the same kind of proliferation of cartilage is present in the cartilage-shaft junctions as that observed in children who have rickets.

Osteomalacia occurs most frequently during gestation and lactation. When the disease does occur in nonpregnant women or in men, it is not severe.

The beginning of the symptoms of osteomalacia are not definite because the patient has been weakened by repeated gestations or by a debilitating disease. It is not until a deformity of the spinal column or distortion in shape of some other bone or bones is observed that the condition can be suspected clinically. The disease may be detected when a roentgenogram is made of a fractured bone

The diagnosis of rickets can be made by clinical examination The diagnosis of osteomalacia is established by roentgenologic examination Both diseases are confirmed in advanced cases by roentgenologic examination The concentrations of serum calcium and serum phosphate are normal or low The serum alkaline phosphatase concentration is often increased during the active stages of both diseases.

Milkman's syndrome differs from osteomalacia only quantitatively It illustrates that an osteomalacia may exist when the only evidence of the presence of the disease is the multiple transparent stripes of absorption or zones of decalcification present in long and flat bones revealed by roentgenologic examination

Rickets and Osteomalacia Secondary to Other Diseases (*Avitaminosis D*). The symptoms of avitaminosis D may be superimposed upon some other disease. Rickets or osteomalacia may develop in a patient who has a capricious appetite and therefore does not eat, or who is able to take a sufficient amount of food but owing to steatorrhea and diarrhea loses vitamin D, calcium and phosphorus in the feces

In rare instances the patient may be resistant to vitamin D Vitamin D resistance may be observed in celiac disease, sprue, chronic jaundice or chronic pancreatitis. In these patients steatorrhea is often present to a severe degree

The loss of calcium and of vitamin D in the feces may explain the occurrence of rickets and osteomalacia in patients who have nontropical sprue.

In certain instances of defective function of the lower nephron with decreased renal functional activity, excretion of calcium in the urine is increased and osteomalacia or rickets may ensue In these patients there is an increase in the serum chlorides, a moderate decrease of serum calcium and a great decrease in the serum phosphorus The carbon dioxide of the serum too may be decreased.

Roentgenograms may reveal multiple regions of calcification limited to the renal pyramids.

For diagnosis of rickets or osteomalacia occurring in association with or sec-

or low phosphorus concentration An increased concentration of alkaline phospha-tase of the serum is present in active rickets or osteomalacia.

Hypervitaminosis D (*Vitamin D Poisoning*). The administration of large doses of vitamin D may be attended by metastatic calcification in the kidneys, bronchi, alveoli of the lungs, mucous membrane of the stomach, blood vessels, and

the group average is then expressed as pounds overweight or underweight. All these standards involve some major uncertainties The designation "healthy" in the reference group means only the absence of obvious disease and defect, and all persons in the reference group are presumed to be equally healthy. Further it is assumed implicitly that the average connotes the best

The main concern in all examinations of height and weight is the proportion of the body represented by fat In very emaciated and in very obese persons the principal difference is in the amount of fat Outside of these extremes the relation of fat to weight is less exact In the ordinary person with no great extreme of either emaciation or obesity, there is no correlation between true fatness and the degree of overweight or underweight calculated from height-weight tables.

True ideal weights are not known The level at which loss of weight or departure from standard average becomes important is not known Tables 22-1 and 22-2 give average weight for specified height and age

The rate at which weight is lost in undernutrition is of consequence In general, it seems that the more rapid the loss of weight the more serious is the disability at equal total losses of weight

The Specific Gravity of Healthy Men. Corporeal density can be accurately measured provided a correction is made for the air in the lungs. The values for specific gravity for healthy men ranging in age between 20 and 40 years are between 1 021 and 1 097 Behnke and associates believe that if it were required that the specific gravity of the body be not lower than 1.060, the obese would be excluded

Low values for specific gravity indicate obesity and, conversely, high values denote leanness Difference in the circumferential measurements of chest and abdomen, when the abdominal circumference exceeds the thoracic, serves as a criterion of obesity and can be correlated with specific gravity. In the absence of obesity the variation in the percentage of bone in relation to body weight may not produce more than small deviations. Individual loss of body weight is associated with an increase in specific gravity

The method for the determination of the specific gravity of the body mass is not generally feasible, in practice, but these investigations temper enthusiasm for too strict adherence to height-weight tables in diagnosis of fatness or leanness.

Obesity. Obesity is an abnormal increase of fat in the tissues In origin obesity may be alimentary, metabolic or endocrine The influence of heredity in the origin of obesity is difficult to evaluate. There is a definite heritable characteristic in human families This characteristic is known as the somatic type. The somatic type is genotypic (see Races, Chapter 16)

The observation that somatic type is a heritable character is not limited to the genus homo A common and well-known field wherein somatic type is of great importance is the breeding of hogs For the production of good bacon it is known to be essential that pigs be selected which have long bodies, these will produce a good-sized corner gammon, prime back and flank The pig with the long body requires more muscle for support of the abdominal viscera than does the pig with the short body Consequently the muscles of the abdominal wall must be larger and thicker, therefore there will be wider lean streaks in the bacon

In a study of more than 500 obese children in Stockholm, Sweden, where the population possesses racial homogeneity valuable for such investigations, Mossberg observed no thyrogenous obesity, and cerebral disease could be implicated in only 19 cases The study revealed that more obese children have obese parents than do normal children, and that the more obese the child, the more likely is one or both parents to be obese, especially the mother, that familial predisposition could result from either constitutional or environmental factors, but that a constitutional heredofamilial factor definitely exists and is common; and that children from families with more than one obese member are likely to become obese before the age of 6

ing of the conjunctiva cannot be used as the main indication of chronic vitamin A deficiency. Darby continued his discussion by pointing out that if such limited criteria were admissable as indicative of vitamin A deficiency a large part of the population who belonged to the middle and older age groups would be judged as having vitamin A deficiency Ophthalmologists have known and have described the conjunctival changes common in presenile or senile patients, but they do not believe that these changes are due to vitamin A deficiency. These conjunctival alterations are subepithelial infiltrations, the epithelium being unaffected, and they may occur in the presence of normal concentrations of vitamin A in the blood. Furthermore, vitamin A therapy in persons showing such conjunctival thickening is entirely without effect. Similar diagnostic errors ensue if hyperkeratosis follicularis is not differentiated from keratosis pilaris Keratosis pilaris is described by dermatologists as a common disease in children less than 12 to 13 years of age; the disorder is not related to a lack of vitamin A, nor does it respond to vitamin A therapy.

Corneal vascularization was, at one time, considered to be due to riboflavin deficiency Although corneal vascularization does occur in ariboflavinosis, the incidence is not necessarily correlated with the riboflavin intake or with other signs suggestive of riboflavin deficiency, and the condition may not respond to therapy with large doses of riboflavin

Darby continued with the enumeration of other physical signs that may be erroneously interpreted as indicative of a specific nutritional deficiency disease. He mentioned that cheilosis as evidence of riboflavin deficiency, glossitis as indicative of pellagra, swollen and bleeding gums as significant of scurvy, and neurologic manifestations alone without other manifestations are of limited value in the detection of nutritional deficiency diseases Important additional knowledge besides these physical findings comprises the dietary and medical history, and results of laboratory studies and therapeutic tests

FATS AND OBESITY

The Nutritive Value of Various Fats. There has been no agreement about the nutritional merits of various fats It is suggested by some that milk fat possesses a specific nutritive quality not present in vegetable fats. Others contend that experimental evidence shows that the vegetable oils possess all the nutritive qualities of milk fat (butter) Experimental evidence is now at hand which from the point of view of clinical significance suggests that nutrition may be well served by both milk fat and vegetable fats Economy and general effectiveness dictate that milk fat, the most easily obtained of the fats, is best taken in the form of whole milk, for whole milk supplies all the valuable nutrient essentials of milk, including butter fat

Digestibility of Fats. Fat yields 9 3 calories per gram in metabolism and is therefore the richest source of food energy Furthermore, the absorption of some fat is essential for the entrance of certain of the vitamins into the body. Reliable scientific evidence shows that fat is as well digested as [illegible] proteins if not better, and that the source of the fat is of lit[illegible] ld be made between real digestibility and satiety [illegible] at.

Body Weight and Fat. In the diagnosis of fatness or leanness dependence on whether or not loss of weight or gain in weight has been sustained is usually based on the height-weight relationship. This means comparison with some set of standards. It is essential to recognize the derivation and limitations of such standards. Since there are as yet neither theoretic nor experimental bases for establishing ideal or optimal relationships between height and weight, recourse is had to averages of supposedly healthy groups which are taken as the standards. The body weight of a given person is then compared with the average of a group of healthy persons of the same sex, age and height. The difference between the individual and

obesity and all leanness are alimentary, is some partially formulated irony The physician suspects that he has not told the whole story The irony will remain until due consideration is given to somatic types, to the fat and the lean, and the heritability of these characteristics.

Table 22-2. Average Height-Weight-Age Table (Women)*

Age	4' 8"	4' 9"	4' 10"	4' 11"	5'	5' 1"	5' 2"	5' 3"	5' 4"	5' 5"	5' 6"	5' 7"	5' 8"	5' 9"	5' 10"	5' 11"	6'
15	101	103	105	106	107	109	112	115	118	122	126	130	134	138	142	147	152
16	102	104	106	108	109	111	114	117	120	124	128	132	136	139	143	148	153
17	103	105	107	109	111	113	116	119	122	125	129	133	137	140	144	149	154
18	104	106	108	110	112	114	117	120	123	126	130	134	138	141	145	150	155
19	105	107	109	111	113	115	118	121	124	127	131	135	139	142	146	151	155
20	106	108	110	112	114	116	119	122	125	128	132	136	140	143	147	151	156
21	107	109	111	113	115	117	120	123	126	129	133	137	141	144	148	152	156
22	107	109	111	113	115	117	120	123	126	129	133	137	141	145	149	153	157
23	108	110	112	114	116	118	121	124	127	130	134	138	142	146	150	153	157
24	109	111	113	115	117	119	121	124	127	130	134	138	142	146	150	154	158
25	109	111	113	115	117	119	121	124	128	131	135	139	143	147	151	154	158
26	110	112	114	116	118	120	122	125	128	131	135	139	143	147	151	155	159
27	110	112	114	116	118	120	122	125	129	132	136	140	144	148	152	155	159
28	111	113	115	117	119	121	123	126	130	133	137	141	145	149	153	156	160
29	111	113	115	117	119	121	123	126	130	133	137	141	145	149	153	156	160
30	112	114	116	118	120	122	124	127	131	134	138	142	146	150	154	157	161
31	113	115	117	119	121	123	125	128	132	135	139	143	147	151	154	157	161
32	113	115	117	119	121	123	125	128	132	136	140	144	148	152	155	158	162
33	114	116	118	120	122	124	126	129	133	137	141	145	149	153	156	159	162
34	115	117	119	121	123	125	127	130	134	138	142	146	150	154	157	160	163
35	115	117	119	121	123	125	127	130	134	138	142	146	150	154	157	160	163
36	116	118	120	122	124	126	128	131	135	139	143	147	151	155	158	161	164
37	116	118	120	122	124	126	129	132	136	140	144	148	152	156	159	162	165
38	117	119	121	123	125	127	130	133	137	141	145	149	153	157	160	163	166
39	118	120	122	124	126	128	131	134	138	142	146	150	154	158	161	164	167
40	119	121	123	125	127	129	132	135	138	142	146	150	154	158	161	164	167
41	120	122	124	126	128	130	133	136	139	143	147	151	155	159	162	165	168
42	120	122	124	126	128	130	133	136	139	143	147	151	155	159	162	166	169
43	121	123	125	127	129	131	134	137	140	144	148	152	156	160	163	167	170
44	122	124	126	128	130	132	135	138	141	145	149	153	157	161	164	168	171
45	122	124	126	128	130	132	135	138	141	145	149	153	157	161	164	168	171
46	123	125	127	129	131	133	136	139	142	146	150	154	158	162	165	169	172
47	123	125	127	129	131	133	136	139	142	146	151	155	159	163	166	170	173
48	124	126	128	130	132	134	137	140	143	147	152	156	160	164	167	171	174
49	124	126	128	130	132	134	137	140	143	147	152	156	161	165	168	172	175
50	125	127	129	131	133	135	138	141	144	148	152	156	161	165	169	173	176
51	125	127	129	131	133	135	138	141	144	148	152	157	162	166	170	174	177
52	125	127	129	131	133	135	138	141	144	148	152	157	162	166	170	174	177
53	125	127	129	131	133	135	138	141	144	148	152	157	162	166	170	174	177
54	125	127	129	131	133	135	138	141	144	148	153	158	163	167	171	174	177
55 and up	125	127	129	131	133	135	138	141	144	148	153	158	163	167	171	174	177

* When taking measurements remove the outdoor clothing, shoes and coat. Age is taken to the nearest birthday For those of slender-frame somatic type deduct 10 pounds and for those of large broad-frame somatic type add 10 pounds (Reprinted from Medico-Actuarial Mortality Investigation, Vol 1, New York, 1912.)

Alimentary Obesity. Alimentary obesity is storage of fat in excess of the normal amount. It is not always easy to demonstrate that the patient indulged in excessive eating Overeating in many instances results from an innate appreciation

years, while in the families of those who become obese after 6 years there are usually fewer than 2 obese members

It remains, however, to be demonstrated in man whether the gene or the environment is the more important factor in the production of obesity. It has been

Table 22-1. Average Height-Weight-Age Table (Men)*

Age	5′	5′ 1″	5′ 2″	5′ 3″	5′ 4″	5′ 5″	5′ 6″	5′ 7″	5′ 8″	5′ 9″	5′ 10″	5′ 11″	6′	6′ 1″	6′ 2″	6′ 3″	6′ 4″	6′ 5″
15	107	109	112	115	118	122	126	130	134	138	142	147	152	157	162	167	172	177
16	109	111	114	117	120	124	128	132	136	140	144	149	154	159	164	169	174	179
17	111	113	116	119	122	126	130	134	138	142	146	151	156	161	166	171	176	181
18	113	115	118	121	124	128	132	136	140	144	148	153	158	163	168	173	178	183
19	115	117	120	123	126	130	134	138	142	146	150	155	160	165	170	175	180	185
20	117	119	122	125	128	132	136	140	144	148	152	156	161	166	171	176	181	186
21	118	120	123	126	130	134	138	141	145	149	153	157	162	167	172	177	182	187
22	119	121	124	127	131	135	139	142	146	150	154	158	163	168	173	178	183	188
23	120	122	125	128	132	136	140	143	147	151	155	159	164	169	175	180	185	190
24	121	123	126	129	133	137	141	144	148	152	156	160	165	171	177	182	187	192
25	122	124	126	129	133	137	141	145	149	153	157	162	167	173	179	184	189	194
26	123	125	127	130	134	138	142	146	150	154	158	163	168	174	180	186	191	196
27	124	126	128	131	134	138	142	146	150	154	158	163	169	175	181	187	192	197
28	125	127	129	132	135	139	143	147	151	155	159	164	170	176	182	188	193	198
29	126	128	130	133	136	140	144	148	152	156	160	165	171	177	183	189	194	199
30	126	128	130	133	136	140	144	148	152	156	161	166	172	178	184	190	196	201
31	127	129	131	134	137	141	145	149	153	157	162	167	173	179	185	191	197	202
32	127	129	131	134	137	141	145	149	154	158	163	168	174	180	186	192	198	203
33	127	129	131	134	137	141	145	149	154	159	164	169	175	181	187	193	199	204
34	128	130	132	135	138	142	146	150	155	160	165	170	176	182	188	194	200	206
35	128	130	132	135	138	142	146	150	155	160	165	170	176	182	189	195	201	207
36	129	131	133	136	139	143	147	151	156	161	166	171	177	183	190	196	202	208
37	129	131	133	136	140	144	148	152	157	162	167	172	178	184	191	197	203	209
38	130	132	134	137	140	144	148	152	157	162	167	173	179	185	192	198	204	210
39	130	132	134	137	140	144	148	152	157	162	167	173	179	185	192	199	205	211
40	131	133	135	138	141	145	149	153	158	163	168	174	180	186	193	200	206	212
41	131	133	135	138	141	145	149	153	158	163	168	174	180	186	193	200	207	213
42	132	134	136	139	142	146	150	154	159	164	169	175	181	187	194	201	208	214
43	132	134	136	139	142	146	150	154	159	164	169	175	181	187	194	201	208	214
44	133	135	137	140	143	147	151	155	160	165	170	176	182	188	195	202	209	215
45	133	135	137	140	143	147	151	155	160	165	170	176	182	188	195	202	209	215
46	134	136	138	141	144	148	152	156	161	166	171	177	183	189	196	203	210	216
47	134	136	138	141	144	148	152	156	161	166	171	177	183	190	197	204	211	217
48	134	136	138	141	144	148	152	156	161	166	171	177	183	190	197	204	211	217
49	134	136	138	141	144	148	152	156	161	166	171	177	183	190	197	204	211	217
50	134	136	138	141	144	148	152	156	161	166	171	177	183	190	197	204	211	217
51	135	137	139	142	145	149	153	157	162	167	172	178	184	191	198	205	212	218
52	135	137	139	142	145	149	153	157	162	167	172	178	184	191	198	205	212	218
53	135	137	139	142	145	149	153	157	162	167	172	178	184	191	198	205	212	218
54	135	137	139	142	145	149	153	158	163	168	173	178	184	191	198	205	212	219
55 and up	135	137	139	142	145	149	153	158	163	168	173	178	184	191	198	205	212	219

* When taking measurements remove the outdoor clothing, shoes and coat Age is taken to the nearest birthday For those of slender-frame somatic type deduct 10 pounds and for those of large broad-frame somatic type add 10 pounds (Reprinted from Medico-Actuarial Mortality Investigation, Vol. 1, New York, 1912.)

easy for physicians to put the blame for obesity and likewise for leanness entirely on the patient by constantly reminding the patient that *all* obesity and *all* leanness are alimentary in origin. Underlying the partial truth of this aphorism that all

deference to objective data on its effects and action It is true that many obese persons have a low basal metabolic rate, but if the results of the basal metabolic test are recalculated in accordance with the ideal weight of the patient rather than his total weight, it will be found that the metabolic rate is either normal or slightly elevated The pharmacologic effect of thyroid in stimulating the combustion of fat may be effective, but often the dose approaches toxic levels. The administration of thyroid to an obese person may result in a loss of weight, but there may be a rapid regain because the intake of food has not been controlled adequately In many instances the patient may take large amounts of the drug without the desired effect. In a few patients there may actually be an increase in weight due to the development of a bigger appetite through the toxic effects of thyroid, productive of nervousness and irritability.

The gonads control the distribution of the fat of the body to conform with the sex of the individual The gonads do not control the degree of general obesity.

Often patients will escape from social competition or responsibility because of their obesity These factors are not specific causes for overeating, but they influence the release of nervous energy into the channel of overeating in those persons who tend in that direction

There has been much publicity in the lay magazines in recent years warning the public against the harmful effects of benzedrine (amphetamine) These harmful effects have been vaguely termed overstimulation of the heart, addiction and nervous upsets It is true that a certain type of person with chronic fatigue, who receives significant mental and physical stimulation from this drug, may find a constant need for it and thereby have an addiction to it much the same as that acquired for many other commonly used drugs Warnings against amphetamine for patients with hypertension have been made by the Council on Pharmacy and Chemistry and the Food and Drug Administration

The Heart in Obesity. Among obese persons embarrassment of the heart and circulation is prone to occur There is an excess amount of fat deposited beneath the epicardium This adipose tissue may encase the heart partially or completely and penetrate into the musculature of the heart The penetration occurs between the muscle bundles and, at times, between the muscle fibers, but not into the muscle cells The right ventricle always is involved to a greater extent than the left ventricle This status impairs the function and nutrition of the myocardium

The increase in body weight by obesity increases the work of the heart The increase in adipose tissue throughout the body and the increase of body surface associated with obesity require an extension of the arterial periphery which, in turn, imposes greater work on the heart

Disturbances of Cellular Lipid Metabolism (Xanthoma, Xanthomatosis, Reticuloendothelial Lipidosis) ***Xanthoma.*** Xanthomas usually are localized infiltrations of the skin and viscera, and they may be primary or secondary. In either case the xanthomas increase in size by addition of cells, not by cell division. The contained lipid gives them their yellowish color A xanthoma heals by undergoing fibrosis and scar formation

Xanthomas of the skin, termed xanthoma tuberosum, appear as small yellowish tubercles with predilection for the extensor surfaces Similarly xanthoma tubercules may invade the vascular system, larynx, lungs, tendons and synovial membranes. When the gallbladder is the site of xanthomatosis, it is known as strawberry gallbladder Complete obstruction of the common bile duct by xanthomas occurs Angina pectoris may follow involvement of the coronary arteries.

Xanthomatosis. It has been stated that xanthomatosis may be either primary or secondary

The *primary xanthomatoses* are characteristically diseases of childhood, though they sometimes occur in adults, and are considered to be congenital errors in lipid

of good food, exquisitely prepared, and artistically arranged on the table and served.

There are many factors which intensify the appetite Some of these are unconscious, while others are recognized by the patients and can be controlled by them When the urge to eat is dependent on unconscious tensions, the patient cannot restrict the intake of food Some of these unconscious drives are so powerful that no incentive for reduction of weight can induce the patient to refrain from overeating. Commonly a patient will say "I would rather die than starve." This attitude is much the same as that of the repentant alcoholic addict who realizes that he is a social disgrace but can do little to control his appetite for alcohol Similarly the tobacco habit is controlled with difficulty, even though a patient may be advised that it is injurious to his or her health

Anything which increases the emotional tonus, such as sorrow, nervousness, irritability, anxiety or an emotional upset, may increase the desire for food. In others, emotional upsets, anxiety, irritability and sorrow will create anorexia nervosa with ensuing sitophobia Persons who have a tendency to be obese eat larger meals or eat more frequently when nervous or worried, or eat more when they are idle, bored or tired A few such examples are found in families in which some of the adult members are overweight Men who conduct their affairs over the dinner table are constantly exposed to rich foods and are influenced to overeat. Women who spend time at cards may obtain excessive calories from the candy, cake and ice cream which are served.

In the presence of a lack of interests or distractions from dullness, escape may be sought in eating This occurs in housewives who break the daily routine by eating frequently It is also seen in such persons as traveling salesmen, who drive long distances and vary the monotony of their trips by stopping for food every hour or so. A great many overeat when they are idle and away from the distracting influences of work

Patients who are confined to the bed or whose activities are restricted may continue to eat according to the habits established when they were active and will thus put on weight because of the temporary decrease in their expenditure of energy Any condition, for instance, an anemia, which induces fatigue may result in a condition of inertia and in relative overeating and obesity.

Anything which makes a patient worried or anxious, such as a social upset, domestic difficulty, or illness or death in the family, may result in overeating However, a loss of weight is considered to be, and is, the classic response to such an occurrence.

Endocrine Obesity. The designation endocrine obesity is used to describe the regional situation of the excess fat For instance, in pituitary obesity, Frohlich's syndrome, and gonadal and adrenal cortical disturbances the fat is characteristically distributed (see discussion of these diseases in Chapter 14). The abdomen, upper arms, and thighs may show accumulations of fat while the face remains thin and the calves and ankles, feet, forearms and hands maintain trim lines. The whole upper part of the body and arms may remain thin and the lower half become fat. Fat in the face and neck is seen in disorders associated with pituitary basophilism of Cushing. These features alone are not diagnostically important in endocrine disorders In fact, some of these distributions of fat may be the result of the so-called lipoid dystrophies which are of unknown etiology.

Only in rare cases is obesity of endocrine origin. The two commonest endocrine dysfunctions found to be responsible for overeating are the climacteric, which results in an increased nervous tension and thus leads to overeating, and premenstrual tension, which also increases tension but which occurs for only about one week before menstruation Puberty and pregnancy are conditions which commonly precipitate overeating through the development of anxieties, fears and new drives

Thyroid for the reduction of weight has been used in tremendous quantities in

Large masses of the characteristic tissue may form within the cranium giving rise to symptoms indistinguishable from those due to neoplasm. Optic atrophy, papilledema, convulsions and palsies of the cranial nerves are sometimes present

Roentgenologic examination reveals large irregular regions of destruction of the bones of the skull, pelvis and extremities.

The diagnosis depends on the presence of exophthalmos, diabetes insipidus, defects in the skull, and xanthomas. Increase of the blood lipoids, especially the blood cholesterol, loss of teeth, and the stomatitis are diagnostically helpful However, biopsy with histologic study is the only conclusive diagnostic procedure. In about one third of the cases the disease is fatal.

Gaucher's Disease This disease is neither definitely familial nor definitely hereditary. It is characterized by enlargement of the spleen and the liver as a result of deposits of kerasin in the reticuloendothelial cells.

The spleen, liver, lymph nodes, bone marrow and sometimes other tissues are infiltrated by large round cells with one or more small nuclei. The cytoplasm of these cells is distended by accumulations of fine granules which do not stain easily and which are believed to be composed of kerasin. The brain contains lesions which resemble those of amaurotic idiocy.

Several siblings are likely to be affected The onset is usually enlargement of the spleen before the first year of life has passed However, the disease may occur at any age and in the aged There are personality changes such as apathy and slowing of movement The eyes do not function properly though there is no failure of vision and the optic fundi are normal The face becomes immobile and the mouth is held open Pseudobulbar phenomena are prominent with attacks of laryngospasm, stridor, difficulty in swallowing, and trismus. There may be an increase of muscle tone and the tendon reflexes

In adults the disease is more chronic than in children The nervous system may or may not be involved. The skin is often deeply pigmented. Anemia is a characteristic feature There may be splenomegaly, hepatomegaly and hemorrhagic tendencies Spontaneous fractures and conjunctival thickenings ensue.

Sternal aspiration or puncture of the spleen and histologic examination of the tissue removed is the preferred method to establish the diagnosis Niemann-Pick disease is distinguished from Gaucher's disease only by studies of the difference in the staining reactions of the lipoid deposits.

In all cases the disease is believed to be fatal within a year or more.

Laurence-Moon-Biedl Syndrome. The Laurence-Moon-Biedl syndrome consists of mental deficiency, retinitis pigmentosa, hypogenitalism, obesity and polydactyly and appears to be inherited as a recessive trait.

Morgagni-Stewart-Morel Syndrome. The Morgagni-Stewart-Morel syndrome (hyperostosis frontalis interna) is inherited as a dominant character. It is manifested by internal hyperostosis of the frontal bone and by headache. The headache is a constant feature Frequently the disease is manifested by obesity, impotence, amenorrhea, benign hypertensive cardiovascular disease, hirsutism, psychosis of indefinite nature or psychoneurosis, fatigability and weakness, and sometimes by disturbances in olfaction, Bell's palsy, diplopia and amblyopia. There is no good evidence of endocrine dysfunction or of a disturbed fat metabolism which might cause the obesity

Diagnostically it is important to remember that hyperostosis frontalis interna or benign frontal exostosis is a common condition which is without clinical significance

Lipodystrophy. Lipodystrophy may be of either congenital or acquired origins.

Lipochondrodystrophy (Hurler's disease, gargoylism), is a rare congenital and familial disease characterized by dwarfism, skeletal deformities, a large head, with grotesque dwarflike face, clouding of the corneas, kyphosis, stiffness of the joints,

metabolism since each of them is distinguished by an excess storage of a particular lipid in the reticuloendothelial system in the spleen, liver, lymph nodes, bone marrow and other organs. These diseases are associated with a particular type or types of lipoid deposits in the reticuloendothelial cells and with the name of a man or the names of two or more men. Some of these may be enumerated: phosphatide lipoidoses (Niemann-Pick disease) in which lecithin and sphingomyelins are deposited in all tissues including those of the nervous system; cholesterol lipoidoses (Schuller-Christian disease) in which cholesterol and its esters are deposited in membranous bones, connective tissues, and in the brain where it is associated with demyelination, and cerebroside lipoidoses (Gaucher's disease) in which kerasin is deposited in the spleen, liver, lymph nodes, bone marrow and nervous system.

Secondary xanthomas occur in the presence of other diseases when there is a disturbance of cholesterol metabolism Xanthomas may involve the skin of a diabetic patient A less extensive xanthomatous involvement of the skin is seen in obstructive jaundice, myxedema, hypertension, and nephrosis The concentration of cholesterol in the blood may or may not be increased

Lipidosis. Under the heading lipidosis or neuronal lipidosis some of the xanthomatoses also are included The diseases included under all of the foregoing headings are (1) Niemann-Pick disease, (2) Schuller-Christian disease and (3) Gaucher's disease The neuronal lipidoses add to the list many more names which will not be considered here In addition to these diseases common in the categories of xanthomatosis and lipidosis are the Laurence-Moon-Biedl syndrome and the Morgagni-Stewart-Morel syndrome

Niemann-Pick Disease This is a familial disease of Hebrews There is an enlargement of the liver and the spleen due to deposits of lipoids in these organs, and sometimes there are lesions in the nervous system.

Girls are affected more frequently than boys The onset is often between the third and the sixth month of life, and almost always before 1 year of age. Brown pigmentation of the skin is often mixed with a waxy pallor.

Both liver and spleen are palpably enlarged Symptoms referable to the nervous system when present are identical with those of amaurotic idiocy. There are mental deterioration, blindness and eventually generalized paralysis and spasticity The cherry red spot in the retina is considered rather characteristic The blood lipoids may be increased. The disease proves to be rapidly fatal

The diagnosis is suspected in Hebrew children in whom enlargement of the liver and spleen develops prior to 1 year of age Sternal aspiration or puncture of the spleen and the demonstration of foam cells is conclusive.

Schuller-Christian Disease. This disorder, known also as *essential xanthomatosis, lipoid reticuloendotheliosis*, and *Letterer-Siwe disease*, is characterized by destructive lesions in the membranous bones and in other tissues. The lesions contain foam cells filled with lipoids There is often present the triad of defects in the skull, exophthalmos and diabetes insipidus, and retarded growth

The disease affects boys more frequently than girls and has no racial preferences or familial tendencies It begins in childhood, often with fever and yellowish or bronze discoloration of the skin There are deposits of the xanthomatous cells in the eyelids, and in the skull, giving rise to soft tumor-like swellings over the cranium There may be symptoms of involvement of the tuber cinereum and the hypophysis such as failure of sexual development, obesity of specific type, diabetes insipidus and Frohlich's syndrome Deposits in the orbits may cause exophthalmos, paralysis of the extra-ocular muscles and optic atrophy. The teeth are often imperfectly formed and may fall out.

The blood is low in hemoglobin and often contains an excess of total lipoids which is sometimes due to a very high blood cholesterol The liver and the spleen are not enlarged as in Gaucher's and Niemann-Pick disease.

SYMPTOMS There is the history of long duration of the intermittent passing of many soft, copious stools possessing a greasy or oily appearance and the ability to float on water. Loss of body weight, weakness and anorexia are important symptoms Muscular cramping of the hands (carpopedal spasms) and the feet is often present, as are severe pains in the arms and legs The abdominal discomforts experienced by some are severe Many of these patients have been on opiates for relief. The abdominal discomforts are variously situated but often they are in the right side of the abdomen

EXAMINATION On examination the evident loss of weight may be the only finding In the presence of tetany positive Chvostek and Trousseau signs are elicited and the blood calcium concentrations are decreased.

The skin is dry, often pale and glistening Frequently, scattered bruised spots appear which are part of a hemorrhagic tendency, noted fairly often in this disease. This tendency is probably related to the deficient absorption of vitamin K As an expression of an avitaminosis B, the tongue may be reddened along its edges and stomatitis is present At times there are cheilosis and dermatitis like those of pellagra. Polyneuritis may be present Some of the younger patients have lens opacities. Edema may be absent, slight or advanced Skeletal lesions observed on roentgenologic examination are osteomalacia, rickets, dwarfism, bending deformities and spontaneous fractures There may be an increased concentration of serum phosphatase in some patients who have steatorrhea.

In the blood there may be microcytes and elongated poikilocytes. There may be some macrocytes and polychromatophils, which indicate a feeble effort to form hemoglobin-containing corpuscles The number of these cells is increased after the administration of iron Reticulocytes are normal in number. An occasional normoblast and microblast may be found The hemoglobin is reduced out of proportion to the erythrocyte count and volume of packed red cells. The erythrocyte count may be normal or even somewhat above normal when the hemoglobin is as low as 8 gm per 100 ml of blood It is the hemoglobin and the volume of packed red cells which reach the low levels The platelets are usually normal in number and small The plasma protein content is often reduced. The leukocytes may be normal in number or slightly reduced Achlorhydria is a common finding The bone marrow is hyperplastic and shows a relative as well as an absolute increase of normoblasts

Some patients with this disease have a fasting hypoglycemia. The blood sugar during a glucose tolerance test fails to increase above the fasting figure by more than 40 mg per 100 ml of blood These abnormalities in sugar metabolism have some diagnostic import Alimentary glycosuria is very rare in idiopathic steatorrhea

The concentration of the blood cholesterol is low or normal in this disorder The concentration of the plasma protein is often decreased The concentration of albumin in the serum may be critically low Urea nitrogen concentrations are usually low in celiac disease, averaging between 8 and 10 mg per 100 ml. of blood.

The total volume of feces excreted in 24 hours by patients who have idiopathic steatorrhea may be increased To measure the fecal excretion of fat and nitrogen, it is advisable to use a standard test diet (the Schmidt diet). By the Fowweather method of analysis in the normal person not more than 25 to 30 per cent of the total dry fecal matter should be composed of fat. The neutral fat should not exceed 12 per cent of dry matter or 60 per cent of the total fat If the amount of total fat exceeds 30 per cent of the dried stool and 75 per cent of the total fat present is hydrolyzed (soaps and free fatty acids), a fault of absorption is assumed

Sigmoidoscopic and roentgenologic examinations are necessary to eliminate the possibility of ileitis, tuberculous colitis, ulcerative colitis and other organic colonic or small intestinal lesions which may very rarely be associated with steatorrhea.

flexed hands, hepatomegaly, splenomegaly and, in most cases, mental deficiency. The disease seems to be a lipoid disturbance of the germinal plasm transmitted in accordance to mendelian rule. The patients are fragile. They frequently suffer from respiratory infections. The majority have cardiac disease which terminates fatally The clinical diagnosis is easy and is confirmed by the skeletal abnormalities and wide involvement of bones as shown by roentgenologic examination. The prognosis is unfavorable.

Lipodystrophia progressiva (Barraquer-Simons disease) occurs in both infantile and juvenile forms In the infantile form of this disease, beginning at about 6 years of age, girls and boys are about equally affected. In the juvenile form, which is the commoner and begins at puberty, girls are predominantly affected.

The cause of lipodystrophy is unknown The condition frequently follows some acute infection, such as measles, pertussis, influenza, pneumonia, and tonsillitis. It has been suggested that the disease is a disturbance of subcutaneous areolar tissues or trophic nerve mechanism having to do with fat metabolism The marked increase of serum fat after high fat intake, the creatinuria, and the lower dextrose tolerance present in some instances suggest a general metabolic disturbance

There is a progressive loss of subcutaneous fat from upper extremities, thorax, face and neck In girls there may be an accompanying increase in fat over the lower part of the body The buccal fat pad disappears in lipodystrophy. There are no other symptoms The change in personal appearance gives rise to various psychologic disturbances. self-consciousness, tension, phobias and insomnia

Examination reveals no abnormalities until atrophy of the fat is evident After weeks or months the atrophy of fat is complete, and the emaciation of affected areas is in striking contrast to the real or apparent increase of fat elsewhere

The condition is evident. It must be distinguished from organic wasting diseases such as tuberculosis, cancer, and pituitary cachexia, and from adiposis dolorosa (Dercum's disease), in which the fat deposits are asymmetric and painful.

Whipple's disease (*intestinal lipodystrophy*) often occurs in middle-aged men The duration of symptoms before death has usually been from 1 to 5 years, though sometimes longer. A history of "arthritis" affecting more than one joint may be obtained. The disease begins with stabbing central abdominal or epigastric pains Fever is not always present In many instances bleeding by rectum occurs Increasing lassitude, loss of weight, diarrhea and steatorrhea, brown pigmentation of skin and oral mucosa, and hypotension may be present. Anemia, achlorhydria, signs of vitamin deficiencies, hypoproteinemia, ascites and edema may be terminal events.

Insulin lipodystrophy occurred in the early days of the use of insulin Subcutaneous fat disappeared in the region of repeated injections of insulin

Idiopathic Steatorrhea and Nontropical Sprue. Idiopathic steatorrhea, called also celiac disease, nontropical sprue, and Gee or Gee-Herter disease, is the passage of a sufficient amount of fat in the bowel movements to give rise to nutritional defects. Nontropical sprue is the designation for the disease when it occurs in adults.

The following etiologic factors have been postulated (1) a deficiency in pancreatic enzymes; (2) a defect in intestinal absorption related to slowing in the process of phosphorylation, depending on deficient function of the adrenal cortex A diminished activity of the adrenal cortex is also associated with avitaminosis B, (3) deficiency in the secretion of bile and (4) mechanical obstruction to lymphatic channels. Among these etiologies a deficiency of pancreatic enzyme is probably not present. Likewise the rest of these theories cannot be proved

The disease occurs during the early years of childhood as a celiac affection. The adult type, also known as *nontropical sprue*, is more likely to be seen in young adults, rarely occurring in patients beyond middle life. Girls and women are most often affected.

There are trophic changes in the intestinal mucosa, a decrease in the weight of the viscera, and a diminution in the amount of intestinal and subcutaneou[illegible]

SYMPTOMS. There is the history of long duration of the intermittent passing of many soft, copious stools possessing a greasy or oily appearance and the ability to float on water. Loss of body weight, weakness and anorexia are important symptoms. Muscular cramping of the hands (carpopedal spasms) and the feet is often present, as are severe pains in the arms and legs. The abdominal discomforts experienced by some are severe. Many of these patients have been on opiates for relief The abdominal discomforts are variously situated but often they are in the right side of the abdomen.

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The total volume of feces excreted in 24 hours by patients who have idiopathic steatorrhea may be increased To measure the fecal excretion of fat and nitrogen, it is advisable to use a standard test diet (the Schmidt diet). By the Fowweather method of analysis in the normal person not more than 25 to 30 per cent of the total dry fecal matter should be composed of fat. The neutral fat should not exceed 12 per cent of dry matter or 60 per cent of the total fat If the amount of total fat exceeds 30 per cent of the dried stool and 75 per cent of the total fat present is hydrolyzed (soaps and free fatty acids), a fault of absorption is assumed

Sigmoidoscopic and roentgenologic examinations are necessary to eliminate the possibility of ileitis, tuberculous colitis, ulcerative colitis and other organic colonic or small intestinal lesions which may very rarely be associated with steatorrhea.

Dilatation of the colon, amounting at times to a marked megacolon, has been observed in instances of steatorrhea.

DIAGNOSIS. The diagnosis is made by exclusion. Results of roentgenoscopic examination may be very suggestive if the patient did not take mineral oil the day prior to examination The subjective and objective signs in steatorrhea may be caused by a number of diseases.

The differentiation between pancreatogenous and idiopathic steatorrhea may be difficult There is no increase in the excretion of fecal nitrogen in idiopathic steatorrhea

Once the diagnosis is well established, the course is intermittently slow, and progression is certain, until in the final stages the patient cannot be maintained on any program, parenterally or otherwise.

UNDERNUTRITION, MALNUTRITION AND STARVATION

The term undernutrition by definition implies that the patient has had an inadequate food supply or that there has been a failure to ingest, to assimilate or to utilize any or all of the necessary food elements. The term malnutrition implies an imperfect assimilation of the food elements though an adequate caloric intake has been practiced The term starvation implies the act of starving from (1) a lack of food as in famine, (2) failure to utilize any one or all of the food elements or (3) failure to assimilate after ingestion. Starvation therefore is the more general term and usually is employed to designate a widespread food shortage as the result of famine.

Undernutrition and Caloric Requirements. The term caloric requirements is widely used but so far has not been precisely defined and probably cannot be so defined With any reasonable definition the requirement will be dependent on body size, age, sex, climate, occupation, personal habits, previous state of nutrition, and perhaps race

In a given person caloric balance can be maintained over a rather wide range of body weight and caloric intake, and it is not possible to determine whether the optimal condition would be toward the upper or the lower end of a range amounting to perhaps 10 per cent or more of the average body weight Changes in body weight are significant, and a person not previously obese who loses 10 per cent or more in weight and continues to lose weight is clearly calorically deficient as the result of starvation or he is ill from disease

In the United States, studies on caloric intake reveal surprisingly low values in some instances in which there is no clinical indication of inadequacy Therefore, human beings seem to have a varying innate capacity to partake of or abstain from food with or without significant loss or gain of body weight.

Undernutrition is present in the majority of patients who suffer from advanced chronic infections, blood dyscrasias, or neoplasms. Temporary undernutrition results from most severe infectious diseases and from major injuries and surgical operations. Anorexia of some degree is common in all of these conditions. A small supply of *exogenous carbohydrate* suffices to prevent ketosis. Thus ketosis and ketonuria do not ordinarily appear in chronic undernutrition, but ketosis will develop in a few days of fasting Associated with this difference in respect to ketosis are differences in the respiratory quotient, in acid-base balance and in the blood sugar concentration

Of the principal organic constituents of living matter the *proteins* in insufficient amounts are the most important cause of undernutrition because of multiplicity of their biologic functions

The recommendations of the League of Nations and the National Research

Council tend to fix on 1 gm. of protein per kilogram of body weight as the normal requirement for adults More recently, however, after studies on nitrogen balance by the National Research Council, it was decided that a man weighing 70 kg could live on a 50 gm. protein diet and maintain approximately 30 per cent margin above requirements.

Pure protein deficiency, with adequate calories and vitamins, is seldom encountered, and little is known about it That it retards growth and leads to hypoproteinemia and anemia is definite

When an inadequate number of calories are ingested a protein intake to fulfill the usual function of protein metabolism is hindered because protein tends to be used as fuel in place of fat and carbohydrate and therefore does not fulfill its specific function. When an inadequate caloric intake prevails the substitution of protein for carbohydrate in the diet has no effect on the balance, and the nitrogen loss from the body continues

Labile protein reserves (depot nitrogen) in the body are small, and a large negative nitrogen balance for more than a day or two is taken to mean either depletion or destruction of tissue With rest in bed, the panacea in all forms of disease and injury, the nitrogen balance becomes negative on the usual diet. It will become negative even in the absence of disease or injury. On the resumption of normal activity on the same diet the nitrogen balance becomes positive. Rest in bed attended by disease which causes a destruction of tissue may permit a positive nitrogen balance if the protein intake is great enough. Decreases in hemoglobin and plasma protein may occur in infections even though nitrogen balance is normal.

Some of the differences in value of the vegetable and the animal proteins are differences in digestibility and absorption Other discrepancies in these proteins are related to metabolic utilization Inadequacy of an essential amino acid may limit the synthesis of a tissue protein Accordingly, protein deficiency may follow from lack of a single amino acid

The necessity for an essential amino acid is not limited to protein for formation of new tissue The metabolic employment of methionine for detoxication and for the formation of choline and creatine exemplifies this observation Metabolic functions of comparable importance can be assigned to tryptophan aside from its part in formation of tissue protein and promoting growth.

The ingestion of tryptophan increases the content of niacin derivative in the urine, thus indicating that some niacin can be synthesized in the body from tryptophan

The protein fractions of the plasma are (1) albumin, 55 per cent; (2) globulin, 38 per cent, and (3) fibrinogen, 7 per cent The 38 per cent of globulin is composed of alpha globulin, 13 per cent, beta globulin, 14 per cent and gamma globulin, 11 per cent. Traces of protein are left in the mother liquid consisting of hormones, for instance, the follicular-stimulating hormone of the anterior pituitary.

Plasma proteins are normally synthesized from food proteins. In starvation they may be formed from tissue protein Albumin and globulin have different amino-acid patterns Protein having its source in muscle and viscera favors albumin formation whereas protein having its source in plants and grain proteins favor globulin formation The presence of infection depresses both albumin and globulin formation.

In the blood plasma there are two albumins and three globulins—alpha, beta and gamma—in addition to fractions contributing to blood coagulation and blood typing Of the globulins, the gamma fraction is concerned with the phenomenon of immunity, for in this fraction of normal and convalescent plasma are found the substances which give high antibody titer.

Normally the blood plasma contains 3 6 to 5 6 gm. of albumin and 1 3 to 3.2

gm. of globulin (euglobulin 0 7 gm.; pseudoglobulin 1.7 gm.) per 100 ml, giving a ratio of 1 5 to 2 5·1 The total protein concentration of the plasma (albumins plus the globulins) varies from 6.0 to 8.0 gm.

Primary alterations in abnormal states occur more commonly in the albumin than in the globulin fractions of the plasma Variations in the one are usually associated with compensatory changes in the other.

The albumins are formed in the liver, but until recently the origin of the globulins remained uncertain. Various degrees of hepatic damage cause a reduction of the plasma albumin. Antibodies are present in the lymphocytes and it seems that the lymphoid tissue is the site of antibody formation Attempts to separate the antibody portion of the plasma from the gamma globulins have proved unsuccessful. However, antibodies are specific modifications of the gamma globulins and these occur in the lymphocytes, with the antigen serving as the stimulus for the modification of the gamma globulin Thus it appears that the gamma globulins are formed in the lymphoid tissue (see Diseases of the Hemic System, Chapter 12)

A chief function of albumin and globulin is the maintenance of a normal colloid osmotic pressure in the capillaries (25 to 30 mm. of mercury) for a normal distribution of fluids between the blood and the tissues, the crystalloid osmotic pressure of the plasma being balanced by that of the tissue fluids. Since the plasma has a higher protein content than the tissues, there is a tendency for fluids to flow from the tissues into the blood which normally is counterbalanced by capillary blood pressure (16 to 35 mm of mercury) In hypoproteinemia the colloid osmotic pressure in the capillaries and venules is reduced, a condition conducive to the production of edema of nephritis as well as in nutritional edema. The albumin and globulin aid in the regulation and maintenance of a normal acid-base or hydrogen-ion equilibrium of the blood

Manifestations of Undernutrition. *Skin, Hair and Eyes* Undernutrition tends to produce a thin, dry, scaly, inelastic, pallid and grayish skin

At the University of Minnesota, Keys and others conducted an experiment on undernutrition over a period of almost 2 years A substantial proportion of the subjects, young men who volunteered for the study, subsisting on a European type of famine diet, exhibited rough gooseflesh-like areas of skin, most often on the extensor surfaces of the thighs and the upper arms. The condition resembled the follicular hyperkeratitis and folliculosis sometimes associated with vitamin A deficiency. The cause did not seem to be clearly related to the state of vitamin A nutrition

A peculiarity of the skin in starvation is a splotchy, dirty brownish pigmentation, appearing anywhere on the body but most often seen on the face The mechanism of the production of this famine pigmentation is unknown It is not related to nicotinic acid deficiency or pellagra

The hair in starvation is usually dry and dull The eyes look dull and dead On closer inspection it is seen that the sclera and cornea are unusually devoid of blood vessels.

Subcutaneous Tissues The edema of undernutrition is ordinarily only moderate and is of the soft, dependent type This edema is present in the face and the lumbar region in the morning and shifts to the lower extremities during the day. Ascites is not present except when there is severe anemia, intercurrent infection, heart failure or decided hypoproteinemia. The latter appears when the diet is unusually devoid of protein and there is less than 5 gm of total protein to 100 ml. of plasma. During recovery from malnutrition edema tends to appear and disappear, being affected by exercise and posture as well as by the food intake. Recently Berkman and associates have shown that in starvation edema resulting from anorexia nervosa the edema is due to retention of salt and water It is evident from the observations of Keys and his co-workers and, independently, of Berkman, that the edema in these

malnourished subjects cannot always be explained by the old theory of hypoproteinemia.

In regard to the belief that one of the controlling factors in the accumulation of ascitic fluid in persons who have cirrhosis of the liver is the concentration of serum protein, particularly the serum albumin, it is well to be aware of the observations of Hoagland. Hoagland and his associates investigated ascites in patients who had cirrhosis and who had been given a special liver extract They expressed the belief that the plasma protein concentration of patients suffering from hepatic cirrhosis does not solely determine whether ascites will or will not be present (Keys)

Muscular Tissues Muscular wasting is a prominent feature of severe undernutrition Most of the wasting seems to be a result of shrinkage of the individual muscle fibers, but in late stages actual destruction of the cells may occur

In both acute and chronic undernutrition the heart shrinks in volume and in weight, the loss being essentially in proportion to the total loss of weight of the body. In the Minnesota experiment the average gross volume of the heart, at systole, measured from teleroentgenkymograms, decreased 17 per cent when the body weight decreased 24 per cent.

Blood Volume. In the Minnesota experiment the plasma volume remained constant or increased slightly in starvation. In proportion to the body weight however there was a definite blood plethora

Blood Cells In the Minnesota experiment progressive moderate anemia occurred in every man during semistarvation

The erythrocytes tend to become slightly larger; the anemia is of the macrocytic type The cause of the anemia in undernutrition is not clear, iron deficiency is not primarily responsible The possibility that excessive peripheral destruction of the erythrocytes is involved is suggested by the presence of hemosiderin deposits in the tissue A definite but moderate leukopenia is the rule in severe undernutrition

In rehabilitation following prolonged undernutrition the correction of the anemia requires months

The Gastrointestinal Tract Gastrointestinal disorders frequently contribute to the disability and death of famine victims Edema of the mucosa of the stomach and intestine may contribute to the anorexia so prevalent in states of undernutrition

Extreme pathologic changes are often found in the intestinal mucosa of those who have severe undernutrition. An increase in the incidence of peptic ulcer is [illegible]

[illegible]

the rate while at rest

In beriberi there may be bradycardia when the patient is resting, but slight physical exertion initiates tachycardia The bradycardia of starvation is not due to heart block, the rhythm is of the sinus type and is regular

[illegible] undernutrition. These [illegible]

[illegible] ll preserved Though there is a tendency to slight peripheral cyanosis, there are usually no complaints referred to the heart and no signs of impending or actual failure except in the terminal state In starvation it is common to observe fainting and giddiness, particularly in the upright posture.

The restoration of cardiocirculatory function during recovery from undernutrition may be complicated by signs of relative cardiac insufficiency or even congestive failure at the time when the rate of gain of weight and of the basal metabolic rate are advancing most rapidly.

The Basal Metabolic Rate. When the food intake is reduced below the prevailing level for the subject, the basal consumption of oxygen declines, and this alteration

tends to be progressive if the inadequate diet is continued. The progress of the undernutrition itself progressively decreases the caloric deficit so that there is a tendency toward adaptation or compensation.

During the convalescence from undernutrition the basal metabolic rate rises synchronously with the gain in body weight.

Brain and Nervous Tissue. The brain and nervous tissue loses little or no weight during starvation. This does not mean that these tissues are unaffected by undernutrition. The changes in weight are limited because the gross structure is preserved with replacement of cytoplasm, or even of cells, by water. The changes in the spinal cord are similar to those in the brain and may be even more pronounced in the anterior horn cells The peripheral nerves are not immune to the effects of starvation, though the medullated fibers are only slightly affected morphologically.

There is no evidence for a decline in basic intellective capacity. In the Minnesota experiment exhaustive studies on memory, reasoning power, verbal and arithmetical facility, and so on, revealed no changes in spite of the subjective impression of most of the men that their mental powers had been reduced

During nutritional rehabilitation from undernutrition the return of a sense of well-being is associated with an increase in voluntary physical activity. However, the habit of conserving energy is not quickly broken. An effort of will or coercion is often necessary to promote recovery in physical fitness by exercise. In former times when starvation was the prevailing treatment of typhoid fever, a year was frequently required to get some of these patients to resume work

All psychomotor functions deteriorate in severe undernutrition, and the result is a serious impairment in working capacity Simple muscular strength, as measured in a single maximal exertion, declines steadily but not so dramatically as does the capacity for continued muscular exertion (endurance) Neuromuscular co-ordination is impaired by caloric undernutrition, but the relative deterioration is less than in purely muscular capacity

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The morbidity and mortality of tuberculosis are increased by caloric deficiency. Tuberculosis is a most serious disease in the presence of prolonged and severe undernutrition In some viral diseases a state of undernutrition seems to decrease susceptibility to infection, for instance, poliomyelitis

Examination in Undernutrition. The findings on examination for the detection of undernutrition depend on the deficiency or the combination of deficiencies present. It is rare to have undernutrition present which is due solely to a deficiency of calories and proteins Therefore, the findings present in vitamin, caloric and protein deficiencies will be considered here

In niacin deficiency, a pellagrous type of dermatitis may be present If a riboflavin deficiency predominates, there may be seborrheic lesions in the nasolabial folds, behind the ears and in other intertriginous areas of the skin In vitamin A deficiency hyperkeratosis in the hair follicles is present. Deficiencies of vitamin C may be expressed by the presence of subcutaneous hemorrhages. In general vitamin B deficiency there is an ichthyosis over the knees, elbows and perhaps over the buttocks and anterosuperior spines of the ilia

The angles of the mouth may be fissured in riboflavin deficiency. The angles of the mouth, also the oral cavity, the tongue and the buccal surfaces may be affected by a scarlet, inflammatory-appearing process in niacin, vitamin B_{12}, riboflavin, and ascorbic acid deficiencies In chronic long-standing deficiencies of these substances, especially of vitamin B_{12} (pernicious anemia), atrophic glossitis and atrophy of the buccal mucous membranes may be found

In vitamin D deficiency there are aberrations in metabolism of calcium and phosphorus, and subsequent skeletal deformities (rickets).

The eyes in vitamin A deficiency may reveal xerosis conjunctivae and xerosis of the corneas A keratoconjunctivitis of the vascularizing variety may be present. Central ophthalmoplegia and retrobulbar neuritis occur as the result of vitamin A and vitamin B deficiencies. The value of the dark adaptation test is not certain.

Bilateral symmetric polyneuritis and subacute disease of the posterolateral column result from deficiencies of vitamin B Disease of the posterolateral column is often present in pernicious anemia as the result of vitamin B_{12} deficiency.

Diagnosis of Undernutrition. The diagnosis of undernutrition depends (1) on dietary history, (2) on medical history and results of physical examination, with attention directed toward the manifestations of nutritional deficiency and (3) on results of certain special examinations The history of the patient's dietary intake permits an estimation of the probability of the presence of a deficiency disease.

Chemical analyses of the blood for changes in the values for serum protein and albumin-globulin ratio, serum calcium, phosphorus, alkaline phosphatase and blood prothrombin time (vitamin K) are regularly employed Their respective normal values are discussed in the appropriate places in this text

When the manifestations and thus physical findings of the classic forms of malnutrition, whether from inadequate caloric protein intake or from lack of vitamins, are present, the diagnosis is obvious However, early forms of these diseases have no specific manifestations For instance, the symptom of ease of fatigability is a constant symptom of pellagra, tuberculosis and, most of all, of psychoneurosis The same may be said of anorexia The diagnosis of a dietary deficiency disease is established by the exclusion of other diseases

At times special examinations can be of help in establishing the diagnosis These tests vary in their significance, in the stage in the development of a specific deficiency which they are capable of detecting For instance, those which measure the concentration of a vitamin in the blood or its rate of excretion in the urine are really indicators of the state of saturation of the body stores, and unless their results are correlated with other evidence, cannot in themselves demonstrate that the deficiency has progressed to the point of impairment of function Unfortunately, most of the methods which are capable of detecting disturbance of chemical or physiologic function are relatively nonspecific Their chief value is often as confirmatory evidence of the clinical findings, and in following the changes which occur in response to therapeutic trial It is evident that the accurate diagnosis of undernutrition is still largely in the province of alertness to the possibility of its occurrence.

Often the therapeutic test—that is, giving specific treatment and observing its effects—may be the only means of determining whether or not the patient's complaints are due to lack of a particular food factor. Obviously, it is important that an adequate amount of food or vitamins must be given and for a sufficiently long time if the therapeutic test is to be of value in making the diagnosis

Starvation, Exposure, and Neglect. The physician sees two common forms of starvation, exposure, and neglect [illegible] in elderly or weak-minded persons wh[illegible] [illegible]e in poverty, dirty, unkempt, often ve[illegible] [illegible]ul neglect of children often is accompanied by their starvation

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Hyperproteinemia due to an increase of plasma globulins occurs in multiple myeloma, amyloidosis, and occasionally in lymphogranuloma venereum, kala-azar, malaria, filariasis, schistosomiasis, trypanosomiasis, leprosy, syphilis, sarcoidosis and the leukemias.

Fibrinogen. The fibrinogen concentration of the plasma is not affected by fasting or by the protein content of the diet so it is not affected by changes in the protein reserves and undernutrition.

Plasma fibrinogen is increased in infections and after trauma if the liver functional activity is normal. It influences the sedimentation rate of the blood.

Fibrinogen is concerned with blood clotting. The plasma contains from 1.9 to 3.3 *gm per 100 ml.* When blood is *drawn from a* vein the fibrinogen is converted to fibrin by the newly formed thrombin.

BENCE JONES PROTEINURIA

Bence Jones protein is a constituent of normal bone marrow, and perhaps leukocytes are concerned in its production. It is an endogenous protein with such a small molecular weight and size that it can easily escape in the urine. Formerly its presence in the urine was considered pathognomonic of myeloma It does occur in the majority (66 per cent or more) of those who have multiple myeloma. It may occur in other conditions such as osteogenic sarcoma, osteomalacia and carcinomatous metastasis to the bone It may be present in the urine of those who have either a lymphoid or a myeloid leukemia. It has been observed in the urine of patients who have pyelonephritis. It may be present in the urine from unknown causes.

OXALURIA

The excretion of excessive amounts of oxalic acid as calcium oxalate in the urine is called oxaluria Normally, the acid occurs in acid, alkaline or neutral urine in crystalline forms A heavy glycosuria is associated with a decreased excretion of oxalic acid

The deranged gastric digestion of carbohydrate that occurs in achlorhydria results in the formation of oxalic acid in its free form which is readily absorbed and

... Calcium oxalate stones most frequently form in the renal pelves and are hard and rough. *Such stones due to their rough surfaces* find it difficult to pass through the ureter even when the stone is small.

Tenosynovitis referable to the precipitation of calcium oxalate ...

... oxalate in the greatest concentration.

URATURIA

Uric acid is an end product in purine metabolism and is excreted in the urine as sodium, potassium and ammonium urates. These urates ...

the urine unless the ...

the

are ... However, in such diseases as gout and

leukemia, in which there is increased excretion of uric acid, no calculous formation occurs, because the organic acid is held in solution as a salt.

Uraturia does not produce symptoms unless uric acid crystals are present in

tion or malnutrition with some superimposed infection than as a state of simple gross starvation There are dehydration and a loss of subcutaneous fat, reaching states of extreme emaciation. The skin is thin, dry, sometimes fissured and sore, and drawn tight over the bony prominences The cheeks are hollow, the eyes sunken, the abdomen is carinated, and the legs and arms are but skin and bones. Pigmentation may vary from mere sallowness to distinct melanosis. The organs are atrophied and the walls of the stomach and intestines are thin, almost transparent, from disuse. Only the gallbladder is enlarged, filled with unwanted bile; the intestines lack the waste matter and chyle which might have caused them to empty.

Great care must be taken to exclude natural disease as a contributory cause or even as a sole cause for such changes Obstruction of the esophagus or stomach, even functional obstruction like the Plummer-Vinson syndrome, and wasting diseases such as tuberculosis, diabetes, Addison's disease, or hyperthyroidism are excluded Starvation and neglect are words which the physician should never use on a death certificate, for they have far-reaching consequences They demand inquiry, must be referred to the coroner, and will undoubtedly necessitate necropsy at his direction Postmortem examination will help to confirm the suspicions aroused, or, on the contrary, will reveal some natural disease which affords a satisfactory explanation of the state of the body

Without food the body loses about a twenty-fourth of its weight each day, and survival is unlikely to continue after about 10 days. If water is provided, life may be prolonged for as long as 50 or 60 days

Hypoproteinemia (Less Than 6.0 gm. per 100 ml. Plasma). A reduction in the total amount of proteins in the plasma is designated as hypoproteinemia. Hypoproteinemia may result in the production of edema because of a reduction in the colloid osmotic pressure of the plasma and particularly since there is but little evidence of an effective compensatory increase of fibrinogen. There are variations in the degree of hypoproteinemia in relation to edema because of the influences of tissue and plasma sodium chloride balance and acid-base equilibrium However, it appears that a reduction of total protein to less than 5.5 gm. per 100 ml. favors the presence of edema Hypoproteinemia, with reduction of serum albumin, may occur in the loss of protein by the excessive and prolonged albuminuria of acute nephritis as well as in chronic active glomerulonephritis, the reduction possessing prognostic significance in acute glomerulonephritis In advanced cirrhosis of the liver with or without ascites the serum albumin may be decreased, although sometimes there is an actual increase of the serum globulin The increase in serum globulin may be ascribed to coexisting malnutrition or to impairment of the liver in the synthesis of the plasma proteins. Hypoproteinemia with decrease in albumin and increase in globulin is common in acute hepatitis and especially in acute yellow atrophy of the liver.

Partly owing to low protein intake, hypoproteinemia is commonly present in states of malnutrition such as diabetes mellitus, anemia, malignant disease, and tuberculosis It occurs in states accompanied by excessive loss of protein in prolonged diarrhea or vomiting; in lipoid nephrosis; sometimes during pregnancy and lactation, in the toxemias of pregnancy, and sometimes in congestive heart failure with edema and anasarca.

Hyperproteinemia (More Than 8.0 gm. per 100 ml. Plasma). An increase

tion from diarrhea, intestinal fistulas, severe vomiting as in high [illegible] obstruction as well as after marked restriction of fluid intake, and in diabetic acidosis High protein values are obtained in extensive burns and in the rare disorder designated Addison's disease.

Congenital porphyria is a rare inborn error of metabolism, inherited as a recessive mendelian characteristic. It is characterized by excretion of large amounts of uroporphyrin, by discoloration of the teeth and bones by these pigments, and by sensitivity of the skin to light.

Often the first symptom is a pink or red or black color of the urine, which may darken after exposure to light The enamel of the deciduous teeth and sometimes the bones of the hands become brown to pink. The bone color is revealed by transillumination

Ultraviolet radiation brings out the cutaneous lesions in childhood. The eruptions consist of brownish pigmentation of the skin, erythema, papules, vesicles and perhaps large bullae filled with a colorless or blood-stained fluid These lesions are situated on the hands, neck and face. The bullae heal with scar formation. In some patients there is hirsutism Enlargement of the spleen and the liver is observed as the disease progresses.

The susceptibility for development of *acute porphyria* has been observed in successive generations, and it is commoner in women than in men. It is inherited as a mendelian dominant characteristic

Acute porphyria with prior manifestations may commence with abdominal colic, constipation and vomiting The colic or neuralgia-like pains may extend down the legs Soon there may be associated with the pains drop foot and wrist drop or a symmetric progressive ascending paralysis of the Landry type. Disturbances of the cranial portion of the central nervous system may consist of amaurosis and facial nerve paresis. Psychic disturbances may occur and the patients may become delirious Death from respiratory failure may rapidly ensue.

Acute porphyria may be associated with a polymorphonuclear leukocytosis and in its manifestations resemble an acute appendicitis or other acute abdominal emergencies. Prior to surgical intervention, if porphyria is suspected, the urine should be boiled with 25 per cent hydrochloric acid, and if porphyrins are present an intense black color develops Porphyria or an acute hemolytic crisis is suspected if there is an intense dark red-brown discoloration of the urine. Demonstration of uroporphyrin in the urine is a definite proof of porphyria. Demonstration of uroporphyrin may be difficult because of simultaneous presence in the [illegible] of a [illegible] luble

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The *chronic forms* of porphyria run a prolonged course and are characterized by a heavy urinary excretion of porphyrin and usually by sensitivity to light These phenomena may follow the prolonged administration of the barbituric acid compounds.

Porphyrinuria may be initiated by sulfonamide compounds, arsenicals, alcohol, phosphorus, selenium and lead Anesthesia, hemorrhage and destruction of tissue may place an additional load on the already disturbed metabolism, and collapse and death may follow. Gastrointestinal symptoms such as cramps, vomiting and constipation occur episodically in chronic porphyria. The urine is dark. Chronic porphyria may prove fatal. In those who survive, recovery is usually slow. In contrast to acute porphyria, in which the porphyrinuria clears up in about a month, the porphyrinuria in chronic porphyria may persist.

The diagnosis of porphyria depends on the [illegible]onstration of excessive amounts of [illegible] a red urine before boiling with [illegible] boiling with hydrochloric acid

an abundance of uric acid. The symptoms then are those of urethral irritation or calculous disease. Restriction of the purine-containing foodstuffs lowers excretion of urate. Alkalization of the urine may be beneficial treatment.

CYSTINURIA

The amino acid cystine occurs in small amounts in the urine of normal persons The designation cystinuria implies an excessive secretion of cystine. All but small amounts of cystine are normally changed into urea and inorganic sulfates before excretion. The cystinuric person possesses the ability to break down cystine, but there is present an inborn error in the intermediary metabolism which permits of excessive excretion

The error in intermediary metabolism occurs in both sexes, at all ages, and follows a recessive mendelian characteristic It has been reported in three generations of a family. A positive family history was present in half the cases studied by Hammer and Thompson

Cystinuria, unless excessive, does not cause symptoms When symptoms appear, if at all, they are those of calculi which have formed in the urinary tract. Cystine lithiasis is a disease of the young, and occurs in only a very small percentage of cystinuric individuals The stones frequently are multiple and bilateral, and after removal tend to recur Ureteral colic, hematuria and albuminuria occur. The urine is acid and of a high specific gravity

Diagnosis is established by finding the characteristic hexagonal crystals of cystine in the urine, or by analysis of urinary calculi removed at surgical operation. The inborn error of metabolism cannot be corrected

PORPHYRIA

Porphyrins are pigments which occur in both plants and animals. Protoporphyrin combined with iron and globin is the basis of hemoglobin The two porphyrins which are important in porphyria are coproporphyrin, which occurs in normal feces after having been excreted by the liver, and uroporphyrin, which is found in small quantities in normal urine The uroporphyrin excreted by the kidneys normally is a very small amount Excessive excretion of uroporphyrin and coproporphyrin may be present in the urine and the feces as in the disease porphyria, or it may be a persistent embryonic type of pigment metabolism An increased porphyrinuria occurs in the disease porphyria, in the aged, in diabetes mellitus, in pellagra, after roentgen therapy and in certain occupational diseases.

The identity of chemical substances used in the formation of the porphyrins in the body has not been accomplished It is now known, however, that a number of respiratory pigments, including hemoglobin, the cytochromes and catalase, contain the porphyrin group Porphyrins may be synthesized in vitro from amino-acetic acid and formyl acetone with perhaps amino acids since they contain four pyrrole rings and perhaps include proline Porphyrin synthesis on a human subject, using the isotope tracer technic, has been done by the administration of amino-acetic acid which contained isotopic nitrogen Samples of blood withdrawn at intervals for 99 days revealed a relatively high value for the isotopic nitrogen content, thus demonstrating the participation of amino-acetic acid in the synthesis of porphyrin in the human subject The present indications are that the porphyrins are synthesized in man from relatively simple chemical substances, including amino-acetic acid and possibly acetic acid.

The disease porphyria is classified according to the age at onset, and the rapidity of onset and duration, into congenital, acute and chronic forms.

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Porphyrins in Occupational Diseases. Maloof found that the value for coproporphyrin was increased in almost every instance in which the concentration of lead in the urine was significant (see Lead Poisoning, Chapter 19). Coproporphyrinuria, although consistently observed in workers who absorb dangerous amounts of lead, is not specific for lead poisoning, since it is observed in many other illnesses. A coproporphyrin test, therefore, should not supplant urinary analyses for lead but should be used in conjunction with them. The early detection of coproporphyrinuria makes it possible to prevent clinical lead poisoning. Coproporphyrinuria may be present before there is stippling of erythrocytes in instances of lead poisoning. However, counts of stippled erythrocytes should be conducted along with analysis of the urine for porphyrin Increase in the number of stippled erythrocytes remains a valuable aid in prevention and diagnosis of lead poisoning

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The disease is due to morbid heredity The abnormal genes are transmitted through heterozygotes who themselves do not manifest any symptoms. Consanguinity is not etiologically definitely important. In some instances, however, the parents of the patients have been first cousins

The essential feature is the urinary excretion of about 1 gm. daily of phenylpyruvic acid, a ketonic acid The excretion is usually continuous throughout life and has been observed in infancy. Those affected are imbeciles or idiots.

The distinctive physical features are dwarfing of stature and reduced cephalic diameters as compared with the normal average. Blond hair and blue eyes are common characteristics The quantity of the acid excreted can be increased by feeding either levophenylalanine or dextrophenylalanine The excretion of the acid can be temporarily abolished by a protein free diet.

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Alkaptonuria is a harmless congenital error of protein metabolism, resulting in the excretion of homogentisic acid in the urine The two amino acids which have been implicated as the source of abnormal metabolism resulting in alkaptonuria are tyrosine and phenylalanine which are the source of homogentisic acid

An hereditary etiologic factor has been considered to be important in those who have alkaptonuria. It is now known that consanguinity is not important etiologically The disease is more common in boys and men than in girls and women.

The majority of instances of alkaptonuria are manifested by the presence of the pigment in the urine This anomaly of protein catabolism is only occasionally associated with ochronosis.

The pigment of ochronosis lies in the fibrocartilagenous structures, the scleras, the tendons, and the skin In a good many patients the scleras have a diffuse gray color, and frequently a semilunar or V-shaped patch of pigmentation occurs in each sclera. Sometimes this pigmentation becomes 0 5 cm. in size and is situated midway between the margin of the cornea on the outer or the inner canthus. The color may vary from deep brown to black.

The pigmentation of the cartilages and fibrous tissues is visible only in certain situations, the most characteristic of which is the ear. The skin of the face may be

involved and often is light brown In some patients there is a uniform yellow-brown color with intensification over the cheeks. In other cases the skin is black.

A similar tissue staining is due to the prolonged external application of carbolic acid preparations. In still others staining of the cartilages is associated with melanuria. The melanin that discolors the tissues is a derivative of the protein molecule.

In chronic instances of ochronosis there is a tendency for premature systemic arteriosclerosis to develop, and the involved cartilages show degenerative changes, osteoarthritic outgrowths and ultimately arthropathies with deformities.

The diagnosis is usually made in early life from the dark stains on the diapers. The urine, on standing becomes alkaline and turns from brown to black due to the oxidation of the homogentisic acid. Homogentisic acid reduces the alkaline copper solutions (Benedict's and Fehling's) and thus its presence may be confused with glycosuria. Homogentisic acid does not reduce an alkaline bismuth solution (Mylander's reagent).

In its early stages ochronosis causes only an undesirable staining of the cartilages. The discoloration of the cartilages, especially those of the ear, is best demonstrated by transmitted light

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It is well to define some of the common terminologies employed in expressing the concentration of a substance in a system, for there is some variation in the way in which laboratories may report such concentrations

The concentration of a substance in a system of specified size may be expressed in different units, for instance, *mass* in milligrams, *volume* in milliliters, the number of *molecules* in millimols, the number of *electrical charges* in milliequivalents Likewise the size of the system may be expressed in either mass or volume of the total system, for instance, a substance plus solvent plus all other substances in the system, or mass or volume of the solvent, or the total number of molecules of the system. In clinical practice substances in the blood plasma, blood serum, or any other body fluid are expressed in milligrams per 100 ml. of the particular fluid in question If it should be desired to express a substance in another unit, it may be so expressed

The concentration of substance X, which exists in solution as a positive ion, may be expressed in the following ways.

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In recent years the conventional way of expressing concentration in biologic systems is in millimols per l. or kg H_2O. In many cases it is sufficiently accurate to use l. and kg H_2O interchangeably, however, since H_2O in a system is almost always determined by weight it is preferable always to use *millimols per kg. H_2O* Milliequivalents are then easily obtained by multiplication [illegible]

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Blood cell water	= 710 ml. per liter of cells	(normal arterial)
	= 714 " " " " "	(normal venous)
	= 730 " " " " "	(terminal nephritis)
	= 725 " " " " "	(pernicious anemia)
	= 720 " " " " "	(diabetic coma)

SODIUM, CHLORIDE AND POTASSIUM

The metabolism of sodium, chloride and potassium is intimately related to the water balance and acid-base equilibrium of the body.

Diets inadequate in other respects are almost always liberally adequate in regard to sodium (Na), chloride (Cl), and potassium (K) The average diet in the United States contains 4 to 6 gm of sodium, 6 to 9 gm. of chloride and 2 to 4 gm. of potassium daily. The normal individual can and often does maintain health on much smaller and on much larger intakes. The requirement for potassium is greatest during periods of rapid growth, for it is necessary for incorporation in the new cells In a healthy adult the potassium requirement is almost negligible. This is in sharp contrast with a relatively constantly high intake of sodium and chloride which is desirable throughout life

The concentration of sodium in normal blood serum ranges from 315 to 340 mg per cent (average 330 mg). The potassium concentration is 16 to 22 mg. per cent (average 19 mg.) There is little or no sodium in the red corpuscles, whereas the average concentration of potassium in these cells is about 420 mg per cent. The chloride content of the whole blood normally ranges from 270 to 300 mg per cent (450 to 500 mg per cent sodium chloride) The distribution of chloride between plasma and cells is similar and intimately related to that of carbonic acid. The relationship of concentrations of sodium, chloride and potassium is important in the maintenance of acid-base balances.

In terms of milliequivalents per liter the distribution of base and acid elements in the blood serum is approximately as follows· sodium (Na 142) plus potassium (K 5) plus calcium (Ca 5) plus magnesium (Mg 3) equals a total base of 155 milliequivalents per liter

The total acid in blood serum. chloride (Cl 103) plus carbonic acid (HCO_3 28) plus phosphates (PO_4 2) plus protein (16) plus sulfates (SO_4 3) plus organic acids (3) equals 155 milliequivalents per liter.

The distribution of potassium, sodium, chloride and water between intracellular and extracellular fluids of the body, is influenced by the adrenocortical hormone (cortin) The mechanism of action of cortin in preserving the normal distribution of these electrolytes and water between the extracellular and intracellular phases is not known

Potassium is the chief basic ion of the muscles and of most of the intracellular fluid, whereas sodium is the chief basic ion of extracellular fluids of the body. Although some movement of potassium and water occurs from cells to plasma, particularly when excessive amounts of sodium chloride and water are lost from the body and in disturbances of acid-base balance, the potassium is usually excreted promptly in the urine [illegible]
extracellular [illegible]
ion can entir[illegible]
the functional activity of the cell In low concentrations potassium is excitatory and in higher concentrations it is inhibitory. Under conditions of normal electrolytic balance the effects of potassium are inhibited by calcium

The exact significance of the inequality of distribution of potassium in the cells and sodium in the extracellular fluids and the mechanism whereby it is preserved are not apparent. In recent years it has been learned that there is more flexibility

CONVERSION OF CONCENTRATIONS

Concentration in millimols per liter:

$$\text{millimols/l} = 10 \times \frac{\text{conc. in mg per 100 ml.}}{\text{molecular weight}}$$

Concentration in milliequivalents (hydrogen) per liter.

$$\text{mEq./l.} = (\text{m.Mols./l.}) \times \text{valence}$$

$$= 10 \times \text{valence} \times \frac{\text{conc. in mg. per 100 ml.}}{\text{molecular weight}}$$

Concentration per kilogram water.

$$\text{conc./kg.}H_2O = (\text{conc./l}) \times \text{kg.}H_2O\text{/l.}$$

$$\text{conc./kg } H_2O = 0.997 \times \text{conc./l } H_2O$$

(measurement of volume at room temperature)

When in the judgment of the director of the laboratory it will be advantageous to report the concentration of the substance X in a particular way, he will so do it. In general, however, the laboratory will record the measure of a substance in terms of molecules of that substance and the size of the system in terms of the mass or volume of the solvent, water

CONVERSION FACTORS FOR IMPORTANT ELECTROLYTES

Sodium: $\text{m Mols Na/l} = \frac{\text{mg Na/100 ml}}{2.30} = \text{mEq Na/l.}$

Potassium: $\text{m.Mols K/l} = \frac{\text{mg K/100 ml}}{3.90} = \text{mEq. K/l}$

Calcium: $\text{m Mols Ca/l} = \frac{\text{mg Ca/100 ml}}{4.00} = 0.5 \times \text{mEq Ca/l.}$

Magnesium: $\text{m Mols Mg/l} = \frac{\text{mg Mg/100 ml.}}{2.43} = 0.5 \times \text{mEq Mg/l.}$

Chloride: $\text{m Mols Cl/l.} = \frac{\text{mg Cl/100 ml}}{3.55} = \text{mEq Cl/l.}$

Bicarbonate: $\text{m Mols } HCO_3\text{/l} = \frac{\text{vols \% } HCO_3}{2.24} = \text{mEq } HCO_3\text{/l}$

APPROXIMATE WATER CONTENT OF BODY FLUIDS AND SECRETIONS

It is not necessary always to determine the water content of body fluids and secretions The water content of these fluids can be made by approximation with general limits of error ranging from 0.5 to 1.5 per cent The approximations are made with the assumption that the body fluids are at room temperature, for instance

1 liter urine contains	0.98 kg H_2O	(normal)
" " "	0.99 " "	(polyuria)
" " "	0.97 " "	(nephritis and nephrosis)

1 liter lymph contains 0.975 kg H_2O
" sweat " 0.99 " "
" gastric juice, pericardial fluid, ascitic fluid, bile, succus entericus or cerebrospinal fluid
contains 0.98 kg H_2O

Plasma water and water of plasma exudates, ml. per liter plasma = 980 − (4.75 × gm. protein per 100 ml)

Whole blood water, ml. per liter whole blood = 932 − (2.2 × cell volume %)
= 980 − (5.3 × gm hemoglobin per 100 ml.)
= 980 − (7.1 × vols. per cent of oxygen capacity)

dry skin, parched lips and mucous membranes, and weakness. Mild and then severe mental changes such as profound confusional states and hallucinations ensue

On establishment of the deprivation of water the volume of urine is decreased to 500 to 700 ml. per day and its specific gravity, provided that the renal concentrating power is normal, increases to 1.030 or more Urine chlorides may be slightly increased or [illegible]

In the ea [illegible] the plasma sodium and chloride [illegible] hange in blood viscosity, serum proteins, or hematocrit reading As a result the blood pressure and circulation are well maintained until death is inevitable.

Pure sodium depletion is caused by the inadequate replacement of excessive losses of salt or sodium chloride Since sodium and chloride are lost in approximately chemically equivalent amounts, the acid-base balance is not disturbed. If the acid-base balance should be found to be disturbed, there is more wrong than sodium depletion

Salt is a constant constituent of visible sweat and by this means of excretion large quantities may be lost If excessive sweating is continued and the normal sense of thirst is heeded and large quantities of water are taken, symptoms of sodium chloride deficiency ensue.

Excessive sweating is common in hot climates and as much as 10,000 to 12,000 ml may be lost in a period of 24 hours, particularly by one not acclimated. Losses of sweat are great among campaigning soldiers and those who work in high temperatures in industry

Symptoms of well-established salt depletion consist of lassitude, fatigue and muscle weakness Any food taken by mouth is immediately vomited. There are headache, and unsteadiness of gait and fainting if the patient tries to stand or walk. Too, there are the sunken cheeks and eyes, and the dry skin and mucous membranes, as are observed in pure water deficiency (see Body Temperature Chapter 21).

When salt depletion is severe, the blood pressure is low, the extremities are cold and clammy, and the pulse is feeble and fast In other words, the symptoms of severe salt depletion are similar to those observed in shock. Before these symptoms can develop as a result of salt depletion, there has been an approximate decrease of the plasma volume of 15 per cent A systolic blood pressure of 90 mm of mercury, if due to sodium depletion, is indicative of a reduction in the plasma volume to three fourths of its original volume As the decrease of the plasma volume advances, there is a relative increase in the constituents of the plasma The proteins and the erythrocytes are increased There are increases in blood viscosity and specific gravity which add to circulatory difficulties Under these circumstances, findings on examinations of the blood may not be significant of the degree of salt depletion, there may be, however, an increase in the concentration of the blood urea

Generally, syndromes of pure water depletion and pure salt depletion are not observed There is present a *mixed depletion of salt and water*.

Mixed Syndromes. The mixed syndrome of salt (sodium) and water depletion, better known as *dehydration*, is often accompanied by a disturbance of acid-base balance. The disturbance in acid-base balance is evidence that in addition to dehydration, other factors, such as starvation, associated with an increased production of metabolic acids, loss of free acids or bases from the body, have already occurred.

Acidosis. *Acidosis* is a clinical term which is commonly employed to indicate a decreased concentration of bicarbonate in the blood (normal values 55 to 75 volumes per cent). It may occur as the result of the formation or absorption of acids at a rate exceeding that of their neutralization or elimination or from excessive loss of blood. It may be produced by an increased accumulation of carbon dioxide in the blood (breathing excess amounts of carbon dioxide or inability to expire

of the concentrations of potassium than was formerly believed possible. Potassium is not fixed in its predominantly intracellular position but can move [illegible]

[illegible]

[illegible] plasma when excessive quantities of sodium and water are lost from the body, as in *hemorrhage*, shock, adrenocortical insufficiency, intestinal obstruction and intestinal, biliary or pancreatic fistulas. During increased muscular activities potassium appears in greater concentrations in the blood plasma During rest or anesthesia there is a reduction in the plasma concentrations of potassium.

Sodium, chloride and potassium are concerned with the maintenance of normal water balance and distribution, the maintenance of normal osmotic equilibrium, the maintenance of normal acid-base balance, and the maintenance of normal muscle irritability

The maintenance of normal hydration and osmotic pressure depends in part on the total base content of the body fluids. Since sodium constitutes the largest fraction (142 of the 155 milliequivalents) of the total base of the extracellular fluids, its role is dominant in this function. At any given carbonic acid concentration, the hydrogen ion concentration of the plasma and other extracellular fluids depends mainly on the bicarbonate concentration Since the bicarbonate content depends on the amount of total base present in excess of anions other than carbonic acid, and since chloride constitutes the largest fraction (103 of the 155 milliequivalents) of the total acid of the plasma, it is obvious that the maintenance of the normal pH depends largely on the presence of normal concentrations of chloride and sodium.

Deficiencies of Water, Sodium, Potassium and Chloride. Deficiencies of water, sodium, potassium and chloride may arise from an inadequate intake, from excessive and uncompensated losses, or from combinations of these aberrations of intake and loss

The patient usually has sustained a varying degree of injury from a mixture of inadequate intake and excessive losses So indefinite are the obtainable data on the intakes and losses that often "heads or tails" cannot be made either from the history or from the tangled mass of laboratory data which may be obtained As nearly as is possible the deficiencies of water, sodium, potassium and chloride will be discussed separately as though they occurred in pure form, a phenomenon which is rarely if ever observed in the clinical practice of medicine

Pure water depletion in health is limited to persons lost or forced down on the desert or sea from airplanes, or imprisoned, as from mine disasters or other hazards A normal person can survive without water in a temperate climate from 7 to 10 days.

Even though the intake of water is stopped, there is an inevitable minimal loss of water which continues The continuation of this loss of water decreases the extracellular water and thereby increases the concentration of the extracellular electrolytes The resulting rise in the electrolytic concentration causes an increase in the osmotic pressure which attracts fluid from the cells in amounts which are sufficient to maintain the plasma volume and therefore to keep the circulation functioning in a normal way until the individual ultimately succumbs to the rising tonicity of all the body fluids if artificial replacement is not forthcoming.

In sickness *pure water deprivation* occurs in those who are unable to swallow and in those whose desire for fluids is blunted or annulled by disturbances of the sensorium or by weakness.

The manifestations of water deprivation are thirst and rapid decrease in body weight. The body loses weight at the rate of 2 per cent daily, and a loss of 15 per cent of body weight is usually fatal if due to water deprivation only. The lips, tongue, mouth and throat are dry. The voice becomes hoarse and talking is difficult. Swallowing of solid foods is impossible. Progressively there are hollowing of [illegible]

Wilder water test used for the detection of adrenal cortical deficiency. There is some evidence to indicate that adrenal cortical deficiency is associated with a decreased destruction of, or increased sensitivity to, the antidiuretic hormone

An increased adrenal cortical activity associated with stress (for example, the postoperative state) may result in an alteration of sodium and potassium excretion.

A limitation of tubular function is manifested by a limitation of the capacity of the transport mechanisms to perform osmotic work. For example, glucose is completely reabsorbed when present in the normal concentration in glomerular filtrate, but, if the concentration is greatly increased, the tubular transport mechanism for reabsorption is saturated, and the excess glucose appears in the urine. These tubular transport mechanisms seem to be a specific enzyme function, for after the administration of phlorhizin, glucose reabsorption is prevented and glycosuria occurs in the presence of normal plasma glucose concentrations

The tubular processes of absorption and secretion involve the performance of osmotic work An approximation of the quantity of work applicable to any constituent of urine can be obtained by comparing the concentration of the constituent in the urine with that in the glomerular filtrate

The factors other than the hormones (adrenal cortex and posterior pituitary) and the enzyme (transport) which alter tubular activity are (1) denervation of the kidneys and (2) anoxia and variations in glomerular filtration. For example, unilateral denervation of the kidneys results in increased water and electrolyte excretion. Renal anoxia from increased renal venous pressure decreases sodium excretion without depression of glomerular filtration rate. Variation in the concentration and rate of flow of the glomerular filtrate produces alterations in excretion if tubular function remains unchanged. It is often impossible on the basis of data on excretion of urine to determine the relative role of changes in glomerular filtration and tubular activity in the altered excretion of any particular substances in the urine However, it is axiomatic that the excretion of a cation necessitates the excretion of an equivalent quantity of anions and vice versa

The renal tubules perform important and related tasks: (1) regulate excretion according to the needs of the body and (2) play an important role in the maintenance of a balance between acidic and basic substances in the internal environment Body pH is dependent on a constant ratio of one part carbonic acid to twenty parts bicarbonate in the plasma The lungs control carbonic acid concentration by varying ventilation. The renal tubules help to stabilize the concentration of the bicarbonate. The tubules accomplish this task by conserving all, or nearly all, of the bicarbonate contained in the glomerular filtrate which is equivalent to approximately 1 pound of sodium bicarbonate per 24 hours

The kidneys may conserve base in two ways (1) by conversion of neutral to acid salts and (2) by synthesis of ammonia. For example, disodium phosphate, entering the renal tubules, comes under the influence of a catalytic enzyme system and reacts with carbonic acid to form sodium bicarbonate and sodium acid phosphate The sodium acid phosphate is excreted, and one sodium ion is conserved by the reabsorption of the sodium bicarbonate

The synthesis of ammonia by the distal tubules permits of a supply of ammonia for the conversion of a sodium salt, for example of sulfuric acid, to the ammonium salt. The sodium bicarbonate formed in this reaction is restored to the plasma, and the ammonium salt is excreted [illegible] a person receiving an average diet is 30 to 50 mE[illegible]. The amount of base conserved by the renal tubu[illegible]nerular filtrate to acid urine can be determined by titrating the urine back to pH 7.4 with a base such as sodium hydroxide This measure has been referred to as "titratable acid excretion" and is normally equal to 10 to 30 mEq per day The sum of titratable acid and ammonium excretion has been referred to as the "total renal defense of the bicarbonate reserve." As long as acid production in the body does not exceed the capacity of these mechanisms, the plasma concentration of bicarbonate remains normal.

The components of urine which may be quantitatively deranged in aberrations of acid-base balance are water, bicarbonate, sulfate, phosphate, sodium chloride and potassium.

carbon dioxide as in asphyxia, drug narcosis, asthma, pneumonia, emphysema and congestive heart failure). *When there is a deficiency in the production of alkali* (as in diabetes mellitus, starvation, renal failure, dehydration from excessive vomiting and diarrhea, and *intestinal, biliary, and pancreatic fistulas*), *acidosis ensues.*

Acidemia implies a decreased pH of the blood irrespective of the changes in blood bicarbonate. The normal value *for the pH of the blood is 7.3 to 7.5,* average 7.35

In instances of acidosis from vomiting there is *a severe loss of chlorides from* the plasma. The chloride concentration of the plasma is more severely reduced than the concentration of the plasma sodium and consequently there is *an increase in the* formation of sodium acid carbonate which accounts for the acidosis.

Acidosis follows a sufficient loss of body acid or decrease in the body base that the blood and the extracellular tissues become or tend to become more acid than normal in reaction. Like alkalosis, acidosis may be produced by aberrational functioning of the respiratory apparatus or may result from metabolic disturbances.

Respiratory acidoses are caused by disease of the heart and lungs, asphyxial states and anesthesia A rare cause of this disorder is the breathing of air in poorly ventilated mines, caves or old-fashioned open wells. In the respiratory acidosis there is an increase in the carbonic acid of the plasma.

The common causes for *metabolic acidosis* are chronic impairment of renal functional activity, as in either acute or chronic nephritis, diabetes mellitus, and starvation (from any cause) Metabolic acidosis follows depletion of the plasma of sodium bicarbonate, or it may result from an excessive accumulation of nonvolatile acids in the plasma.

The importance of the *kidneys* in electrolyte balance is obvious when it is realized that in the resting state approximately one fourth of the entire cardiac output passes through the renal vasculature Approximately one fifth of the plasma reaching *the* kidneys is filtered through the glomerular membrane and forms approximately 180 liters *of glomerular filtrate per 24 hours.*

The formation of glomerular filtrate is a physical phenomenon The hydrostatic [illegible] mately

approximately 10 mm of mercury, the actual filtration pressure equals appro[illegible] of 20 mm of mercury Glomerular filtrate is identical with plasma except for the absence *of large molecules such as those of protein. Four fifths of this filtrate is absorbed before* reaching the collecting tubules of the kidney

The *function of the thin segment of the nephron is not clear* Probably its purpose is to permit attainment of osmotic equilibrium by passive back diffusion of water following reabsorption of most of the osmotically active substances in the proximal tubule

In the distal convoluted tubule the antidiuretic hormone of the posterior lobe of the pituitary body normally regulates the rate of tubular reabsorption of water. It seems that a fixed fraction of the filtered fluid and electrolyte escapes the *proximal tubule,* and that in the absence of antidiuretic hormonal activity, all or most of the water reaching *the distal tubule is excreted In posterior pituitary deficiency* (diabetes insipidus), the maximal flow of urine observed equals approximately 15 per cent (27,000 ml) of the glomerular filtrate

Reabsorption of sodium and potassium in the distal tubule is under control of the adrenal cortex Hormones of the type of desoxycorticosterone are effective in causing sodium retention and potassium excretion Hormones of the type *of cortisone* are less effective. Corticotropin (ACTH) acts to stimulate the secretion of these hormones, provided functional *cortical tissue is present* Adrenal cortical insufficiency (Addison's disease) is associated with an increase in sodium excretion and a decrease in potassium *excretion*

Patients who have adrenal cortical insufficiency have a defect in *salt balance and a* decreased diuretic response to ingested water This is the basis for the Power-Kepler-

Wilder water test used for the detection of adrenal cortical deficiency. There is some evidence to indicate that adrenal cortical deficiency is associated with a decreased destruction of, or increased sensitivity to, the antidiuretic hormone.

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The components of urine which may be quantitatively deranged in aberrations of acid-base balance are water, bicarbonate, sulfate, phosphate, sodium chloride and potassium.

The metabolic waste products of the body can be excreted in 600 to 700 ml. of urine per day. When there is excessive production of waste products or a decrease in concentrating power of the kidneys, an increase in volume of urine results or retention of the waste products ensues Starvation, fever and diabetic acidosis are examples of conditions associated with an increase in excretory products Thus with normal renal functional activity the urine becomes dark in color and appears thicker in consistency.

Bicarbonate is the most labile of the plasma anions because of its easy conversion to and formation from carbon dioxide. Its concentration in the plasma is determined by the total concentrations of base and fixed acids. The normal concentration of bicarbonate in plasma is 27 mEq per liter. At lower concentrations than 27 mEq. per liter all bicarbonate through the tubules is reabsorbed At concentrations more than 27 mEq per liter some bicarbonate is excreted. This apparently stable threshold is reduced by hyperventilation and increased in the presence of a low plasma chloride concentration.

Sulfate is for practical purposes quantitatively reabsorbed at normal concentrations and filtration rate. Any increase in the quantity filtered exceeds the reabsorptive capacity, and increased amounts of sulfate appear in the urine. However, a decrease in glomerular filtration with relatively less damage to tubular function may result in inadequate sulfate excretion. In chronic renal disease, sulfate retention occurs earlier than an elevation of blood urea.

There is a definite tubular reabsorptive capacity for phosphate so that this compound is maintained as a constant plasma concentration so long as the rate of phosphate production and filtration rate remain constant. Reabsorption of phosphate by the renal tubules is depressed in the presence of great increases in plasma levels of glucose or certain amino acids with which it shares transport mechanisms

Most of the sodium and chloride is reabsorbed in the proximal tubule It has been mentioned earlier in this discussion that the excretion of sodium and chloride is conditioned by filtration rate, plasma concentration, and hormones of the adrenal cortex and possibly the posterior pituitary There is considerable evidence to indicate that the fraction of filtered sodium reabsorbed in the proximal tubule tends to increase with a decreasing filtration rate and to increase with increases in plasma concentrations. However, excretion is not simply a threshold phenomenon The ability of the tubules to transport sodium is an intrinsic one This rate of transport is regulated by hormonal and other factors Excretion of sodium and chloride not only is influenced by tubular activity but also is dependent on rate of glomerular filtration.

In the absence of any change in body content of water and salt, the daily excretion [illegible] ials ingestion. The average [illegible] The body's mechanism for [illegible] the 140 mEq per liter contained in the glomerular filtrate may be absorbed by the tubules so that the urinary concentration may fall below 1 mEq. per liter.

The amount of potassium excreted is normally less than the amount contained in the glomerular filtrate Secretion of potassium by the tubules can and does occur The present concept is that extensive potassium reabsorption occurs in the proximal tubule and may be supplemented by tubular excretion in the distal tubule and that the distal process, normally small, is increased during increased ingestion or liberation of potassium when increased plasma concentrations prevail

The behavior of potassium in the body is not well known It is for this reason that it is thought that simultaneous reabsorption and tubular excretion of potassium may occur.

The importance of the kidneys in the body economy is made obvious and the disaster which follows the slowly progressive loss of renal functional activity can be observed as a chronic glomerulonephritis advances

Approximately 24 gm of urea, constituting nearly one half of the total solids of the urine, is excreted daily in the urine of a normal person consuming 80 gm. of protein per day.

Urea is completely filtered through the glomerulus; but the amount actually excreted equals only 30 to 60 per cent of that contained in the glomerular filtrate, depending on the rate of flow of urine. The discrepancy between the amount of urea filtered and the amount excreted in the normal person is apparently due to diffusion from the lumen of the tubule through the tubule cells into the blood stream.

Retention of urea in the patient with advanced glomerulonephritis is the result of reduction in the rate of glomerular filtration. The smaller daily volume of filtrate presents a reduced quantity of urea to the tubules, and the slower passage causes an increase in the percentage of the urea which is passively reabsorbed Consequently, the rate of excretion in the urine is reduced The concentration of urea in the blood (and in the subsequent filtrate) therefore rises until excretion equals formation In the early stages of a chronic renal failure, this elevation of the blood urea usually goes unnoticed because of the wide variation in protein intake and the range of the accepted normal

During the early stages of glomerulonephritis tubular function is seldom greatly impaired except in the nephrotic phase of the disease, and even then the proteinuria is believed to be due to an increased permeability of the glomerular membranes.

The relatively slow passage of the reduced volume of filtrate through the tubules permits reabsorption of an abnormally high percentage of sodium and water. The excretion of sodium and water is more greatly reduced than is glomerular filtration. This retention of sodium and water contributes to the edema which may be present in acute glomerulonephritis It is an indication for restriction of sodium intake at this stage of the disease.

A low level of plasma protein (particularly albumin) with retention of sodium results in edema in chronic nephritis and this may be termed the *nephrotic phase* of the disease

The low osmotic pressure of the plasma and the increased glomerular permeability combine to cause an abnormally high rate of glomerular filtration. Apparently there is an even greater increase in rate of reabsorption of sodium and water so that these substances are retained also.

Eventually in the progress of chronic glomerulonephritis, a stage is reached in which there is nitrogen retention in the plasma There is a reduction in renal blood flow, glomerular filtration, and capacity for tubular work Tubular injury seems to exceed the glomerular disorder The diminished capacity for tubular work manifests itself by increased volume of urine having a low specific gravity, impaired or absent synthesis of ammonia, and defective reabsorption of base The latter two defects may result in the loss of large amounts of sodium and potassium Anion retention, especially sulfate, may occur relatively early in the course of renal insufficiency

Necrotizing nephrosis, crush syndrome and lower nephron nephrosis are terms applied to the syndrome involving the kidneys that may follow crushing injuries, transfusion of incompatible blood, poisoning or necrosis of tubule cells. Renal blood flow is impaired by reflex vasoconstriction, and there may be mechanical obstruction of tubules from precipitated heme pigment, from drug (i e, sulfonamide) cellular debris, or from a combination of these substances

Here the presence of anuria does not necessarily mean that glomerular filtration has ceased There is evidence that lack of flow of urine from the kidneys may be due to complete back diffusion or reabsorption of the filtrate into the blood through the walls of the tubules, and anuria ensues.

If the patient survives the anuric or oliguric phase of necrotizing nephrosis, diuresis begins from 7 to 21 days after onset. The diuretic urine may approach the

glomerular filtrate in composition, indicating a lack of selectivity in tubular reabsorption The body thus may be depleted of sodium and especially potassium

In a patient with anuria, from any cause, (1) sodium, potassium, and chloride should be excluded from the diet so far as possible, except for the amounts necessary to replace loss by vomiting, diarrhea, or excessive perspiration; (2) administration of water should be limited to an amount equal to that lost as insensible perspiration, through the lungs, and in the excreta (the water content of food and water of oxidation should be considered in this calculation); and (3) protein ingestion should be at a bare minimum, with an adequate caloric intake to minimize breakdown of body protein

During the phase of diuresis, supplementation of oral intake of water and electrolytes may be necessary to keep up with the loss.

In shock associated with extensive tissue damage (for example, crushing injuries), the release of large quantities of myohemoglobin is a contributing factor. In burns there may be a similar release of noxious materials which may cause intravascular hemolysis. Allergy and disturbances in electrolyte balance may, in some instances, be important in the etiology of acute renal failure.

Chronic congestive heart failure is accompanied with a reduction in glomerular filtration manifested by a decreased capacity for excretion of sodium, chloride, and possibly water

Since the retention of fluid in congestive heart failure is associated with no great change in concentration of sodium or chloride, it follows that water has been retained in a relatively fixed ratio to these electrolytes. That sodium rather than chloride is the important ion is demonstrable by the diuretic effect of ammonium chloride and the increase in edema produced by ingestion of sodium bicarbonate.

In recognition of a decreased capacity for sodium excretion as the primary defect, regardless of its exact mechanism, the obvious therapeutic approaches are (1) limitation of sodium ingestion and (2) use of measures to increase the excretion of sodium Therapeutic means of accomplishing the latter include rest in bed, cardiac glycosides, ammonium or potassium chloride or nitrate, mercurial diuretics, xanthines, and sodium-removing resins

During the course of cirrhosis of the liver and especially when liver function is greatly impaired there is a decreased renal excretion of water and salts manifested by ascites. This tendency toward ascites formation is favored by an increase in portal pressure However, there are other factors concerned with the formation of ascites in cirrhosis of the liver. These factors are: (1) increased pressure in the capillaries of the portal circulation, (2) decreased plasma osmotic pressure, (3) decreased glomerular filtration rate, (4) an increased amount of circulating antidiuretic hormone, (5) increased intra-abdominal and renal tissue pressure and (6) increased capillary permeability. The importance of these factors when taken all together in the production of ascites is definite, for the limitation of the intake of the sodium ion does reduce edema and ascites in cirrhosis as it does in congestive heart failure

The task of regulating the electrolyte concentration of the plasma by the kidneys is great in diabetes because in this disease there are (1) excessive production of acid substances and (2) deficiency of base and water for their removal.

Lack of insulin in some manner results in hepatic production of beta-hydroxybutyric and acetoacetic acids in larger quantities than can be removed by body metabolism and renal excretion. These substances accumulate in the blood and, because of their acidity, displace plasma bicarbonate Excretion of sugar and ketone bodies requires an increased renal loss of water and base (sodium and potassium). The resulting dehydration is often accentuated by decreased food and fluid intake and by vomiting Dehydration, if severe, results in a decreased plasma volume,

hypotension, and decreased glomerular filtration. Thus, the capacity for excreting the accumulating abnormal metabolites is further diminished

On physical examination in acidosis there are observed shallow and irregular respirations and often an increased irritability of the neuromuscular system. The urine at first is alkaline in reaction but as the acidosis progresses it becomes acid

There is a marked decrease in plasma chlorides (normal values 340 to 370 mg. per 100 ml.). In severe acidosis the plasma chlorides may be less than 185 mg. per 100 ml Accompanying the decrease in plasma chloride there is an increase in the plasma bicarbonate to 90 to 110 (normal 55 to 75 volumes per cent). The carbon dioxide-combining power of the plasma decreases so that in slight acidosis it is 55 to 45 volumes per cent, in moderate acidosis, 40 to 30 volumes per cent; and in severe acidosis, 25 to 10 volumes per cent.

Alkalosis. Alkalosis is a chemical term employed to indicate an increased blood bicarbonate with a tendency toward alkalemia The term alkalemia indicates an increased pH (above 7 5) irrespective of the concentration of the bicarbonate of the blood.

The common cause for alkalosis is hyperventilation or overbreathing (sighing syndrome) by the hysteric patient Hyperventilation depletes the plasma of carbonic acid Alkalosis may result from an increased intake of alkalies, as in peptic ulcer, or from a loss of hydrochloric acid

In hysteria often there is a sensation of being unable to breathe or to take a long breath The patient does actually breathe deeply and at an increased rate with a resulting hyperventilation The patient may complain of attacks of "unconsciousness" if the alkalosis is severe In severe instances of hyperventilation Chvostek's sign, Trousseau's sign, cardopedal spasm and vocal stridor may be present. The syndrome is caused by an excessive excretion of carbon dioxide A similar condition may be observed in certain instances of encephalitis.

The metabolic forms of alkalosis are usually more easily identified because of a definite history of ingestion of excessive bicarbonate as in the treatment of peptic ulcer or of vomiting or diarrhea.

When alkalosis is present, there has been a loss of body acid or an increase in body base to a sufficient degree that the blood and extracellular tissues tend to become more alkaline in reaction. In mild alkalosis the carbon dioxide-combining power of the plasma, according to the Van Slyke method, is 70 to 78 volumes per cent (normal values 55 to 75 volumes per cent) which advances with the progression of the alkalosis until a value of 100 or more volumes per cent may be reached

Alkalosis and Tetany. Tetany may be present in alkalosis under the following circumstances. (1) after ingestion of excessive quantities of bicarbonate, (2) after continued pulmonary hyperventilation and (3) after protracted vomiting. The excessive loss of hydrochloric acid results in lowering of the plasma chlorides and increase in bicarbonate

In *bicarbonate tetany* there are an increase in plasma carbon dioxide-combining power and a decrease in concentration of plasma chlorides (gastric tetany).

[illegible]

are unchanged

Water intoxication may be induced in a normal individual by forced ingestion of large quantities of water over a short period of time. It is induced by drinking large quantities of water by an individual who has lost large quantities of sweat. It may occur during the course of diabetes insipidus

Thirst is somewhat conditioned to the ingestion of food. If there is a reduction in the diet, which usually entails a reduction in the intake of salt, and if the reduction in the diet is carried to the extreme so that carbohydrates also are eliminated, there

ensue a salt and water depletion and ketosis. Both salt depletion and ketosis promote dehydration and abate thirst When water alone is taken to replace these deficits, the salt of the body fluids becomes diluted to hypotonic concentrations and the state which follows is known as water intoxication.

The manifestations are variable, however, usually consisting of muscular cramps (see Heat Cramps, Chapter 21), nausea, vomiting, headache, oliguria and convulsions The low salt syndrome of Shaffer is a variant of water intoxication.

POTASSIUM

Potassium is the principal basic ion in the intracellular fluid Aside from its osmotic functions within the cell it possesses functions related to the processes of phosphorylation and deposition of glycogen and the neuromuscular transmission of nervous impulses In the blood plasma in health the amount of potassium varies from 13 5 to 21 5 mg. per cent (3 5 to 5 5 mEq /l.) Departure from this range of normal values may be followed by definite disturbances of neuromuscular functions

Hypopotassemia (Potassium Deficiency) Evidence of potassium deficiency is encountered only as a result of the excessive losses which occur in certain types of illness and also in the condition of familial periodic paralysis In starvation, fever and other conditions which lead to excessive destruction of body protein, potassium, like phosphorus and nitrogen, is excreted in large quantities in the urine In human beings important losses of cellular potassium have been shown to take place as the result of trauma, shock, hemorrhage, severe diarrhea, sprue, diabetic coma, and severe alkalosis due to loss of chloride. Loss of intracellular potassium in excess of that to be expected from protein breakdown is a general response to water depletion from any cause.

The severe vomiting in intestinal obstruction lowers the potassium level The serum potassium may be decreased by protracted vomiting and decreased still further after therapy with saline and dextrose solutions That the depletion involves the serum potassium and intracellular potassium is suggested by the small rise in serum concentration following injection of relatively large doses of potassium chloride

Familial Periodic Paralysis This condition is characterized by recurrent attacks of flaccid paralysis affecting the muscles of the trunk and extremities The majority of cases reported have been members of the same family groups The disease may be transmitted through either men or women who may themselves be free from it

In some cases no significant morphologic lesion can be demonstrated In others the serum potassium concentration falls during the attacks and the symptoms are relieved by administration of potassium salts During the paralytic phase the serum potassium concentration varies considerably in different cases, being usually less than 14 mg per 100 ml. and at times as low as 7.6 mg, although values as high as 17 4 mg per 100 ml have been observed Weakness has been observed to begin, in extremely rare instances, whenever the serum potassium falls below 16 mg per 100 ml Attack may be induced by agents that cause a lowering of the serum potassium concentration, including dextrose, insulin, thyroid extract, epinephrine and ephedrine Excretion of potassium in the urine may decrease markedly during an attack The actual significance of the aberrations in potassium metabolism cannot be interpreted (Duncan).

SYMPTOMS. The disease occurs twice as frequently in males as in females Symptoms usually begin during early childhood or adolescence and tend to become less frequent in later life. First attacks, however, have been reported after 30 years of age. Onset of the attack is often during sleep. If the attack begins during the waking hours, it may be preceded by numbness, formication and fatigue. The paralysis is flaccid and involves all of the voluntary muscles. The muscles of the face, eyes, tongue and organs of speech and deglutition are seldom affected Functions of

bladder and bowels are maintained The deep and superficial reflexes in the affected regions are lost. In severe attacks there is complete absence of reaction to faradic and galvanic stimulation, with a return to normal during intervals between attacks. There are wide variations in the distribution and severity of the paralysis The attacks may last only one-half to 1 hour, but usually persist for a few hours to a few days Motor power and reflexes usually return gradually and the patient feels perfectly well Occasionally the paralysis develops slowly, over a period of a few hours

Diagnosis of Potassium Deficiency. The diagnosis of potassium deficiency is made in the presence of decreased serum potassium concentration when accompanied by the history and findings of starvation and fever from any cause. One of the common causes of potassium deficiency is intestinal obstruction.

The decreased concentration of serum potassium causes the following electrocardiographic changes diminution, depression or inversion of the T wave; the QT interval is prolonged and the ST segment is depressed

Hyperpotassemia (Potassium Intoxication). An increase in the concentration of potassium occurs in acute high intestinal obstruction, uremia, portal cirrhosis with ascites and frequent abdominal paracentesis, severe infections, hyperparathyroidism, in Addison's disease, and in epilepsy and other convulsive disorders.

Flaccid paralyses have been reported to be associated with both low and high concentrations of serum potassium Instances of flaccid paralysis with increased concentrations of serum potassium were not observed by Keith and Burchell in their experience with renal insufficiency The paralysis in uremia is not closely correlated with any critical potassium level of concentration in the serum. Changes in intracellular potassium may occur without obvious changes in extracellular or serum potassium levels

The electrocardiographic pattern is influenced by the intracellular changes in the concentration of potassium For this reason an electrocardiogram serves as a rapid and reasonably reliable index of alterations in intracellular potassium concentration It is useful both in diagnosis and in control of therapy. The sequence of events in the heart muscle as depicted by electrocardiographic studies seems to occur in the following order of appearance increased height of the T wave, a QRS of increased width, loss of P waves; gross intraventricular conduction defects, the electrocardiogram superficially simulating bundle-branch block, cardiac arrest with irregular undulating potentials of low voltage In hyperpotassemia the T wave is exaggerated and eventually the P wave may disappear.

Diagnosis of Potassium Intoxication. The diagnosis of potassium intoxication depends on the presence of paresthesias of the hands and feet after the ingestion of the potassium salts or during the course of severe renal insufficiency and failure. The actual proof of the potassium intoxication rests on the demonstration of a coexisting hyperpotassemia and a characteristic electrocardiogram The plasma concentration of potassium should exceed 21.5 mg. per 100 ml or 5 5 mEq. per liter.

CALCIUM

The normal total serum calcium concentration varies from 8 5 to 11.5 mg per 100 ml ; of this about one half is said to be diffusible calcium The calcium of the blood is contained entirely in the plasma.

The absorption of calcium is decreased by increased alkalinity of the proximal small intestine and by a decreased phosphate content of the chyme with the formation of insoluble calcium soaps, as in obstructive jaundice, sprue and celiac disease.

Hypercalcemia. Increases in the serum calcium or in the plasma calcium occur in hyperparathyroidism, in excessive administration of vitamin D, in diseases of the bone such as multiple myeloma, and occasionally in metastatic carcinoma of the

bone; when there are mild increases in the carbon dioxide of the blood in association with such diseases as congestive heart failure, emphysema, pneumoconiosis and asphyxia; in chronic nephritis, especially during uremia and occasionally in pregnancy. Rare diseases which are uncommon and irregular causes for hypercalcemia are polycythemia vera, Addison's disease, and Cushing's disease

Hypercalcemia, with increased urinary excretion of calcium and phosphorus, may occur as a result of rapid demineralization of bones, especially in the presence of simultaneously impaired renal function Under these circumstances the concentration of phosphate in the serum is either normal or increased

The administration of parathyroid hormone causes an increase in the concentration of the serum calcium and urinary excretion of calcium. Synchronously there are a decrease in serum phosphorus, an increase in urinary phosphorus, and an increase in the serum phosphatase activity The function of parathyroid hormone in maintaining the serum calcium concentration is exerted through mobilization of this element from its storehouse in the bones.

Vitamin D increases the absorption of calcium from the intestine and aids the deposition of calcium and phosphorus in the bones Vitamin D exerts a greater and more immediate influence on phosphorus than on calcium in the blood serum.

Hypocalcemia. Hypocalcemia is one of the most constant and characteristic features of diminished parathyroid function. In some cases of rickets, when infantile tetany develops, hypocalcemia is present. In steatorrhea the serum calcium may be low and tetany, delayed ossification and osteoporosis may occur

Decreased serum calcium values may be associated with hypoproteinemia accompanying the nephrotic syndrome, obstructive jaundice, kala-azar, malignant disease and other cachectic states The diminution in serum calcium occurs entirely in the nondiffusible fraction and is apparently due to the decrease in the concentration of albumin in the serum and not to any disturbance of calcium metabolism.

Hypocalcemia is occasionally observed in nonnephrotic forms of chronic glomerulonephritis in the stage of renal functional failure

The clinical conditions characterized by disturbance of calcium and phosphorus metabolism are those dependent on or associated with abnormalities of parathyroid function and of vitamin D supply or utilization, for instance hyperparathyroidism, rickets, prolonged obstructive jaundice, sprue, celiac disease, hunger osteopathy and occasionally in malignant disease and cachectic states

Tetany. Tetany is characterized by an abnormally increased reaction of the somatic and autonomic motor and sensory nerves to stimuli. As a sequence of these stimuli painful, tonic spasms of groups of muscles or all of the muscles of the body ensue This nerve-muscle phenomenon is due to one or more changes in the body which are associated with alkalosis (which has just been considered in previous paragraphs) or to a reduction in concentration or inactivation of a portion of the serum calcium

Hypoparathyroid tetany follows thyroidectomy or parathyroidectomy and occurs in spontaneous hypothyroidism

Postoperative tetany usually results from the surgeon being unable to discover one or more parathyroid glands during thyroidectomy In rare instances it results from excision of too much parathyroid tissue in parathyroidectomy. Often these postthyroidectomy tetanies are due to temporary suppression of parathyroid function, as a result of trauma, edema or hemorrhage or interference with the blood supply of the parathyroid glands, and they are of brief duration

In those who have tetany postoperatively the symptoms may appear within a few hours, days or even weeks after operation. In the instances in which an interval of several days to a few weeks elapses before the symptoms of tetany appear, there

is often a disturbance of blood supply to the parathyroid glands as the result of fibrous organization of inflammatory exudate or hemorrhage. In these cases the tetany is prolonged or even permanent.

Idiopathic hypoparathyroidism is a rare condition. It has been attributed to inflammation or to hemorrhage into the glands It is chronic and presents essentially the same clinical and metabolic features present in postoperative tetany.

Infantile tetany occurs in rickets It is due to vitamin D deficiency and inadequate intake of calcium. The concentration of serum calcium is decreased The calcium and phosphorus balances are negative or subnormal, owing to excessive loss of these elements in the feces. The serum phosphatase activity is usually increased in proportion to the severity of the skeletal lesions, which vary from mild demineralization to the advanced demineralization present in rickets

Osteomalacic tetany occurs in adults and may be regarded as the counterpart of infantile tetany associated with rickets

In the *maternal tetany* of pregnancy the requirement for calcium, phosphorus and vitamin D is increased, as is indicated by parathyroid hyperplasia If the serum calcium decreases to subnormal concentrations, as it may do occasionally in the late months of pregnancy and during lactation, there will be tetany. The *tetany of the newborn* appears to be related to the existence of tetany in the mother.

Tetany is a common manifestation of *celiac disease, sprue and idiopathic steatorrhea.* It is due to impaired intestinal absorption of fats The calcium unites with these fats, calcium soaps are formed, and large amounts of calcium are thus lost. Impaired absorption of all foodstuffs is hindered by the increased intestinal motility. These abnormalities eventuate in osteoporosis, rickets, dwarfism, osteomalacia, hypocalcemia and tetany The serum phosphorus concentration is also frequently diminished These conditions are usually easily differentiated from other forms of tetany by the excessive fat content of the feces, the presence of anemia and gastrointestinal malfunctions

Tetany from parenteral administration of fluids such as soluble oxalates, phosphates or citrates may result from an induced hypocalcemia Calcium citrate is poorly ionizable and after its administration hypocalcemia does not ensue Tetanic manifestations may follow the intravenous injection of neutral, alkaline or slightly acid sodium phosphate Tetany may occur in advanced forms of renal failure also.

Manifestations of Tetany Tetany occurs in a latent, an acute or a chronic form Latent tetany does not present symptoms, but symptoms may be elicited by stimulation of peripheral nerves Acute tetany is manifested by spontaneous muscular spasms and other manifestations of nervous hyperirritability

Latent Tetany The presence of latent tetany, if there should be any reason for its presence being demonstrated, may be easily detected by mechanical or electrical excitation of the hyperexcitable nerves Electrical or galvanic stimulation elicits Erb's sign, which is a neuromuscular response obtained with weaker currents in tetany than under normal conditions

The Chvostek sign (facial phenomenon), hyperexcitability of the facial nerve to mechanical stimulation, is elicited by tapping the trunk of the facial nerve immediately anterior to the external auditory meatus A positive reaction consists in momentary contraction of the upper lip with associated movement of the nose, or the entire side of the face This sign may occur in normal subjects

The Trousseau phenomenon is elicited by applying the sphygmomanometer with sufficient force to stop the circulation. A positive reaction consists in the production of contraction of the fingers and hand in the obstetric position This sign, like the Chvostek sign, is not pathognomonic of tetany

Acute Tetany. The readily recognizable spontaneous spasms of acute tetany are the carpopedal spasm, laryngospasm and convulsions These may be preceded by and accompanied by paresthesias and intense pain.

In carpal spasm the thumb is inserted into the palm; the fingers, extended at the distal joints, are flexed at the metacarpophalangeal joints; and the wrist is flexed and the hand drawn to the ulnar side. In pedal spasm the feet are extended at the ankle joint in the position of equinovarus. There may be stiffness or spasm and pain in other muscle groups of the extremities. Facial spasm may produce stiffness and rigidity of the face, with the corners of the mouth drawn downward There may be rigidity of the entire body, especially of the neck and back, strabismus, nystagmus, inequality of the pupils and difficulty in speech and swallowing.

Laryngospasm occurs in children and may occur as the result of a very slight reflex irritation such as a cold, emotional disturbance and sudden awakening. There is a loud inspiratory crow due to spasm of the glottis. The attacks vary in severity and frequency and, if repeated, may be accompanied by dyspnea, cyanosis, coma and respiratory failure, which may terminate fatally. Usually the glottic spasm relaxes in a few minutes Diaphragmatic spasm may cause inspiratory or, rarely, expiratory apnea, which may cause death. Bronchotetany may produce attacks simulating asthma, in severe instances there is dyspnea. These respiratory manifestations are relieved by administration of calcium intravenously but do not respond to subcutaneous administration of epinephrine.

Autonomic nerves and smooth muscles may be affected. Spasm has been observed in the iris, the ciliary muscle, and the esophagus, throughout the gastrointestinal tract, and in the bladder Cardiac spasm may cause sudden death Palpitation, tachycardia, and cardiac irregularity occur frequently. Angiospasm results in pallor, especially of the fingers and toes, dermographia and muscle pain. There may be localized regions of puffiness of the skin or edema of the face or of the hands and feet (Duncan).

Chronic Tetany. Hypoparathyroidism is the most important cause of chronic tetany In latent tetany of hypoparathyroidism there may be trophic changes in the hair, skin, nails, teeth, and the crystalline lens of the eye.

The hair becomes coarse in texture and sheds in spots or almost completely. The skin is thickened and roughened and the nails become brittle, ridged, and may be shed The dentin and enamel of the teeth may exhibit small pits and horizontal grooves Both nuclear and cortical lenticular opacities may be recorded by the ophthalmologist on examination with the slit lamp.

The characteristic blood findings of hypoparathyroid tetany are hypocalcemia, normal or increased serum phosphorus concentration, normal serum phosphatase activity, and normal acid-base equilibrium.

Diagnosis of Tetany. The history and physical findings are usually diagnostic Serum calcium concentrations are diminished to 4 to 8 mg. (normal 8.5 to 11 5 mg.) per 100 ml and there is no parallelism between the severity of symptoms and the degree of hypocalcemia Serum phosphorus concentration may be normal (2 to 4 mg per 100 ml) but is usually increased (5 to 10 mg per 100 ml.) The absolute or relative increase in serum phosphorus plays a significant role in determining the precipitation of clinical symptoms of tetany There is a decreased urinary excretion of calcium and phosphorus.

Pathologic Calcification. The term metastatic calcification is applied to the deposition of lime salts in tissues which have not been the site of preceding regressive changes The lesions occur in the tubular epithelium of the kidneys, about acid-secreting glands of the gastric mucosa, and in the alveolar walls and vessels of the lungs, pancreas and other organs. Occasionally there is calcification of the pulmonary veins and the wall of the left auricle, the peripheral arteries, the trachea and the liver, and in some instances all tissues are affected

Metastatic calcification has been observed in hyperparathyroidism, hypervitaminosis D, renal rickets, multiple myeloma, myelogenous leukemia, extensive skeletal metastasis of sarcoma and carcinoma, marble bones and widespread osteomyelitis.

The term dystrophic calcification is applied to deposits of lime salts in dead, degenerated, or devitalized tissue, as in infarcts, regions of necrosis and fatty degeneration, inspissated collections of pus, hyalinized scar tissue, caseating tubercles, and atheromatous patches in the intima of vessels. Dystrophic calcification becomes more extensive in the presence of hypercalcemia, hyperphosphatemia, destructive lesions of bone, and impairment of renal function

Calcinosis is characterized by the deposition of lime salts in and beneath the skin. *Calcinosis circumscripta* is the commonest form of calcinosis In this condition the calcification is superficial, localized to the skin, occurs at any age, usually in the upper extremities, particularly in the fingers, and, because of the resemblance of the deposits to tophi, has been called calcium gout. The concentration of calcium in the blood is not increased.

Calcinosis universalis occurs most frequently before the age of 20 years In this condition there is no regular increase in the calcium of the serum. In addition to deposits in the skin, as in calcinosis circumscripta, widespread deposits occur subcutaneously and in the connective tissue of muscles, tendons, fascia and nerves Calcification may occur in the capsules of lymph nodes. The nodes often coalesce and may break down and ulcerate, discharging a chalklike material Calcinosis of the muscles is termed myositis ossificans (see p 328). Calcinosis about the joints is termed chalk gout.

Scleroderma and manifestations of the Raynaud syndrome, occur in a large proportion of those who have myositis ossificans. Calcinosis circumscripta causes little or no interference with function, but in calcinosis universalis contraction of tendons and muscles interferes with function of joints and muscles, and ulcerations of the skin may become portals of entry for local infections, septicemia, or bacteremia. There are no regular known increases in the blood calcium in these conditions.

PHOSPHORUS

Phosphorus occurs in the blood as inorganic phosphates, as organic phosphates as in the nucleotides, as phosphate esters, and as lipids. In adults inorganic *phosphate in the serum varies normally from 3 to 4.5 mg*, and in infants and young children *from 4 to 6 mg.* per 100 ml of serum The amounts, however, vary directly with the concentration of solar ultraviolet rays, being highest in summer and lowest in winter Following the ingestion of carbohydrates there is a gradual and progressive decrease of serum phosphate which persists during the period of increased glucose utilization, returning to normal in 4 to 5 hours This fall occurs independently of the blood sugar

The concentration of phosphorus in the serum may be increased (5 0 plus mg), *hyperphospheremia,* by therapeutic and by excessive doses of vitamin D, and by irradiation. Increase in serum values for phosphates may occur in hypoparathyroidism, the degree of increase being approximately proportional to the degree of hypocalcemia Hyperphospheremia occurs also in the healing of fractures, chronic

rickets If the concentration of calcium be multiplied by that of phosphorus, each being expressed in milligrams per 100 ml , a product is obtained which, *in the normal child,* ranges from 50 to 60 When the product is less than 30, rickets is usually present, and when it is more than 40, either healing is occurring *or rickets* has probably not been present. These observations cannot be relied upon absolutely.

A primary disease of phosphorus metabolism is commonly observed *in osteitis* fibrosa diffusa due to hyperparathyroidism and resulting from an increased elimina-

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hyperparathyroidism, generalized osteoporosis, hyperthyroidism, osteomalacia, metastatic carcinoma involving bone, osteogenic sarcoma, Hodgkin's disease, lymphosarcoma and leukemia with involvement of bone, polyostotic fibrous dysplasia, during the period of healing of fractures, Gaucher's disease with resorption of bone and osteopoikilosis (osteosclerosis fragilis generalisata, marble bones) and, rarely, in renal rickets and multiple myeloma

Normal serum contains small amounts of acid phosphatase, less than 3 units. *Serum acid phosphatase activity* is increased in carcinoma of the prostate with metastasis. The source of this enzyme under these circumstances is the acinar epithelium of the prostate gland. Carcinomatous prostate tissue also contains large amounts of acid phosphatase, and when metastasis occurs, with invasion of lymph or blood channels, large amounts of the enzyme enter the circulation When there is metastasis to bone, the alkaline phosphatase too may be increased

IRON

The absorption of iron from the gastrointestinal tract is normally a controlled process In the healthy, nondeficient adult only a small portion of ingested food-iron will be absorbed each day In an iron-deficient person the absorptive process is much more efficient, and a high percentage of the ingested iron may be taken up Studies of iron absorption in growing children indicate that the efficiency of the absorption process parallels the need for the element Similarly, during the latter half of pregnancy the absorptive efficiency is greatly increased, this being the period during which the fetal stores of iron are built up

Iron exists in the blood in the erythrocytes and in the plasma or the serum. The iron of the erythrocytes, the hemoglobin, has been discussed in Chapter 12. In the normal total iron content of the blood the organic iron is 52 mg per 100 ml, of which 57 per cent is hemoglobin iron The hematin iron is not available for use The interest here is on the plasma or serum iron

It seems probable that all iron which is absorbed must first be reduced to the ferrous state Ascorbic acid reduces ferric iron, and there is evidence that it may serve this role under physiologic conditions

Absorbed iron is transported in the plasma or the serum in the ferric state as one of the globulin fractions Inorganic iron is that part of the iron which remains in the plasma or the serum and can be determined by special methods The normal range of values for plasma iron or serum iron is usually stated to be about 80 to 180 micrograms per 100 ml Low values are encountered in the hypochromic microcytic anemia of iron deficiency and in the anemia of infection Higher than normal values are present in pernicious anemia and hemolytic anemias

Iron which is given intravenously disappears rapidly from the plasma or the serum It seems that iron thus administered is stored, and it is known as available storage iron The measure of the concentration of iron which can be retained by plasma or serum under such circumstances is spoken of as the iron-binding capacity.

The available storage iron is made up of recently absorbed iron plus that recently released during the breakdown of hemoglobin, and a more fixed, less readily available, tissue iron The chief sites of storage iron are the liver, spleen, bone marrow, and kidneys The tissues contain the so-called parenchymal iron also

Practically no iron is excreted in the urine, and the excretory iron in the feces comprises less than 1 0 mg per day

Requirements for Iron. The times of the greatest requirement for iron are during the first two years of life and the rapid growth of adolescence and, in women, throughout the childbearing period After the menopause the requirement drops. The Food and Nutrition Board of the National Research Council has given estimates that a man weighing 150 pounds (68 kg.) requires 12 mg of iron daily. Twelve

tion of phosphate in the urine. Hypophosphatemia may be present in idiopathic steatorrhea, in tropical and nontropical sprue, and in periods of increased carbohydrate metabolism coincident with large amounts of fats in the intestines and with the defective absorption of calcium, phosphorus and vitamin D. Also hypophosphatemia follows the administration of glucose, insulin, epinephrine and parathyroid extract, and is present in uncontrolled diabetes.

Phosphaturia. All normal persons excrete 1 to 3 gm. of phosphoric acid as an alkaline salt in the urine each day. When this excretion is excessive or when the phosphates are precipitated in the urogenital tract, this condition is termed phosphaturia

Almost all (95 to 99 per cent) of the urinary phosphorus occurs as sodium and potassium phosphates which are soluble in both acid and alkaline urine. The calcium and magnesium salts are insoluble in alkaline urine, and it is therefore these salts and the alkaline urine which are responsible for phosphaturia Phosphaturia is commonly present when there is an excessive ingestion of sodium bicarbonate or of certain fruits with an alkaline ash or when urinary infections and bone diseases occur.

Other than a slight burning on micturition there are no symptoms unless calculi are present The turbidity of the urine due to phosphates occurs only in a neutral or alkaline urine To be significant, the deposit must be heavy in a freshly voided urine

PHOSPHATASE

An enzyme phosphatase which does not contain phosphate is normally present in the bones, kidneys, striated muscles and blood This enzyme liberates inorganic phosphate by hydrolysis of phosphoric esters for the deposition of calcium phosphate in the bones It exists in both alkaline and acid forms

Serum alkaline phosphatase activity is reported from the laboratory in terms of units. A unit of alkaline phosphatase activity as defined by Bodansky is "equivalent to the actual or calculated liberation of 1 mg of phosphorus as the phosphate ion during the first hour of incubation at 37 C and pH 8.6, with the substrate containing sodium beta-glycerophosphate, hydrolysis not exceeding 10 per cent of the substrate "

Phosphatase activity is low at birth, rises to a maximum during the first month of life, and remains fairly high during the second year, the values in later childhood falling gradually to adult levels. High protein diets cause a decrease, and high carbohydrate diets an increase in phosphatase activity of the serum The range of normal values for plasma or serum alkaline phosphatase activity in adults is 1 5 to 4 units per 100 ml and for children 5 to 14 units (Bodansky).

Serum phosphatase activity is increased in a large proportion of patients who have obstructive types of jaundice (to 60 units), portal cirrhosis, metastatic carcinoma involving the liver, and biliary fistula

Increased serum phosphatase activity occurs during periods of calcification of hemorrhages in scurvy, in active tuberculosis and Boeck's sarcoid, and in chronic myeloid leukemia

Serum alkaline phosphatase activity is increased chiefly in certain diseases of bone and in certain disorders of the liver and the biliary tract. In the former it appears to be related in most instances to the extent of osteoblastic activity or to the intensity of attempts at formation of bone

It is consistently increased in active rickets (20 to 190 units) The degree of increase may be regarded as a reliable criterion of the severity of the condition High values (15 to 125 units) are obtained rather consistently in osteitis *fibrosa cystica*, or slightly increased activity (to 25 units) may occur in cases of localized involvement of one or two bones. A moderate increase (20 to 40 units) is observed in

is a consistent increase in its incidence. A decline in the incidence is observed after the age of 55 years. Women are rarely affected before the age of 50 years. The disorder affects men from 20 to 25 times as often as it affects women (Duncan).

Once the hemochromatosis has become established, it is a progressive chronic disorder manifested by an abnormal deposition of hemosiderin in the skin and viscera, cirrhosis of the liver, diabetes mellitus and in some instances by deposition of iron in the myocardium.

SYMPTOMS. Perhaps the most constant manifestation is cirrhosis of the liver. There are lassitude, discomfort in the epigastrium, and a sensation of heaviness and distention in the abdomen due to ascites and enlargement of the liver These symptoms may appear late in the course of the disease but usually are the most significant. In the final stages of the disease hematemesis, purpura, icterus, diarrhea, dyspepsia, and vomiting may be present. The presence of symptoms of a complicating myocardial failure, pulmonary tuberculosis and carcinoma of the liver may render the symptomatology complex and difficult to recognize.

Diabetes mellitus may result from hemochromatosis It is an early manifestation in less than one third of these patients The diabetes mellitus of hemochromatosis is usually controllable for a while In rare instances it may be exceedingly severe from the onset and difficult to control. The patient passes through a state of increasing insulin resistance to one in which insulin is completely ineffective.

Heart block and heart failure are occasional manifestations of a heavy deposit of hemosiderin in the myocardium

Asthenia is a common symptom of hemochromatosis from beginning to end. It may be secondary to disturbances in the function of the adrenal glands, to the cirrhosis of the liver, to diabetes or to myocardial failure

EXAMINATION. The pigmentation of the skin is evident in approximately 8 of every 10 patients who have hemochromatosis It is the first sign of the disease in about one fourth of all who have it The skin is bronzed, bluish metallic, gray, or slate color. The color is more obvious about the genitalia and perineum, and in the folds of the skin, in scars and on exposed portions than elsewhere, but it affects to a degree all of the skin The face, the extensor surfaces of the forearms, and the extensor surfaces of the hands are commonly deeply pigmented Pigmentation of the buccal mucosa occurs in 1 of every 8 who are affected. The conjunctivae also may be pigmented Often there are nail marks from scratching of the intensely itching skin

Xanthoma and xanthomatous eruptions of the skin may be present. Often there is considerable loss of hair from the scalp and the axillary and pubic regions

The liver usually is enlarged, smooth, firm and not tender In late stages of the disease the liver shrinks and cannot be palpated. The spleen is palpable in about one half of the cases Ascites appears frequently as a late manifestation.

A moderate hypochromic anemia, hyperglycemia, hypercholesterolemia, glycosuria, and reduced serum albumin with a reversal of the albumin-globulin ratio are common findings. Abnormal results of tests of hepatic functional activity, particularly bromsulfalein-retention, are present. Icterus, though an unusual complication of this disorder, may be present and cause an increased concentration of the serum bilirubin. Moderate increases of the basal metabolic rate are common.

DIAGNOSIS The diagnosis is most easily made by hepatic biopsy. However, the presence of cirrhosis of the liver, diabetes mellitus and pigmentation of the skin is rarely mistakable for anything other than hemochromatosis

The disorders which may resemble hemochromatosis are argyria and Addison's disease. Pigmentation is the only characteristic which these three conditions have in common The history and physical examination should establish the correct differentiation. Hemochromatosis and Addison's disease do occasionally occur in the same patient.

milligrams of iron daily is required by a nonpregnant woman weighing 123 pounds (about 56 kg.). During the second half of pregnancy and during lactation she requires 15 mg. daily. The requirements for iron increase from 6 mg. daily during the first year of life to 15 mg. daily until the age of 20 years is reached. After the age of 20 years the requirements for adults prevail.

Iron Deficiency. In the infant, iron deficiency is most often of dietary origin. In the adult the deficiency is conditioned by chronic loss of blood.

The clinical evidence indicates that by the time adulthood is reached even the poorest dietary regimens which are likely to be encountered are sufficient to prevent iron deficiency in the absence of chronic loss of blood. Iron deficiency results from repeated losses of blood The commonest sources of these losses are: menorrhagia; bleeding peptic ulcers, hemorrhoids; menopausal menorrhagia; abortion, miscarriage or bleeding after delivery; hookworm disease; and loss of blood secondary to malignant changes in the gastrointestinal tract, in the nasopharynx or in the urogenital tract

The iron-deficient person usually is easily fatigued and listless. Palpitation on exertion, a sore tongue, angular stomatitis and dysphagia may be present, and hypochromic microcytic anemia is usual (the Plummer-Vinson syndrome). Koilonychia may also be seen Any combination of these conditions may be encountered Signs other than the anemia are not usually encountered in children. The oral lesions occur in one degree or another in about 10 per cent of iron-deficient adults Plasma iron levels are low Iron absorption, however, is increased, as can be demonstrated by use of the radioactive iron technic.

The presence of a low hemoglobin level is not alone sufficient for the diagnosis of iron-deficiency anemia, whether in a particular person or in a group of the population. The findings indicative of the anemic state may be cardiac abnormalities such as hemic murmurs, cardiac enlargement, symptoms of angina pectoris, palpitation and even electrocardiographic changes. Dyspnea and edema are not infrequently observed.

Hemochromatosis *(Bronze Diabetes). The cause of hemochromatosis is obscure* Minute quantities of iron in excess of body needs are retained and accumulate over a period of years The retention may be due to an inherited abnormal inability of the cells to rid themselves of iron

Hemochromatosis has been observed to occur as the result of a familial and hereditary predisposition. Whatever the cause, there is an abnormal retention of iron The total iron content of the body may be from 5 to 10 times the normal content of 3 gm in the normal person

In hemosiderosis iron pigments deposited in the tissues are used again in the formation of blood, whereas in hemochromatosis the hemosiderin is not used again Hemosiderosis originates from excessive destruction of blood. In no stage of development of hemochromatosis is there detectable evidence of excessive erythrocyte destruction

Hemosiderin as well as some hemofuscin are deposited in the propria of the sweat glands and in the deeper strata of the malpighian layer of the skin The liver is enlarged and the capsule is thickened The surface is firm and nodular and there are accumula- [illegible] ated with [illegible] tion and actual loss of acinar and islet tissues Deposits of hemosiderin are present in the spleen, the lymph nodes, the pituitary, thyroid, and salivary glands, and in the myocardium. Hemofuscin is found in the cells of glandular organs, in *connective tissue*, in smooth muscle, and particularly in the walls of the medium-sized and small arteries

The melanin of the deeper layers of the epidermis is increased in amount The skin coloration in this disease is not due to deposit of excessive iron-containing pigments

Hemochromatosis occurs in patients between the ages of 45 and 55 years The condition is unknown before the age of 20 years but from this age to 40 years there

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The prognosis in hemochromatosis depends on how well the cirrhosis of the liver and the diabetes mellitus respond to treatment in the absence of cardiac complications After diabetes mellitus is fully manifested life rarely lasts more than 1 year.

GLYCOGEN DISEASE (GLYCOGENOSIS)

Glycogen disease is rare It is inherited as a mendelian recessive character. This disorder of metabolism is characterized by the storage of normal glycogen within the liver, heart and kidneys, and usually by retardation of growth and of the development of sex characteristics

As a result of the immobility of the hepatic glycogen, the systemic blood sugar concentrations are low, 60 mg. per 100 ml. or less. There are no hyperglycemic symptoms A glucose tolerance test reveals a moderate delay in glycogen storage and a retarded return to a mild hypoglycemic level. There is a tendency toward acetonuria owing to incomplete oxidation of fat.

The first symptom is enlargement of the abdomen. The liver is enlarged and smooth The kidneys too in some instances are enlarged and easily palpated

In an obese child the findings of a low fasting blood sugar value, acetonuria, and an increased concentration of cholesterol in the blood (up to 400 mg per 100 ml) in association with hepatomegaly are suggestive. The epinephrine test fails to reveal the usual rise in the blood sugar. The glucose tolerance curve is abnormal The concentration of glycogen in the blood is increased Sudden death may occur from severe hypoglycemia or from cardiac failure.

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23

THE AUTONOMIC (VEGETATIVE) NERVOUS SYSTEM

References have been made to functional disorders which occur in association with most of the organs and all of the systems of the body. The remarks in regard to these disorders imply a diagnosis of a psychoneurosis or a disorder attributable to aberrations in psychic control. When a diagnosis of a psychoneurosis is made, too frequently all of the manifestations or queer reactions of the patient are attributed to the psychoneurosis. Cold wet hands, hypersensitiveness to heat and cold, change in the size of the pupils and often pupillary reactions, aberrations in tendon reflexes, irregular respirations, irregular heart beating, digestive disturbances and many other irregularities are considered as a part of the prevailing psychoneurosis However, some of these manifestations are present in normal persons. When these manifestations are found in the normal individual without being the subject of complaint they are dismissed by the experienced physician. These manifestations may be the source of needless examinations, perhaps treatment both operative and medical by the [illegible]

It does not matter whether the patient has a psychoneurosis, is enjoying good health without complaints or whether he is organically sick, if he has cold wet hands, hypersensitiveness to heat and cold, irregular sweating over various parts of the body, vasomotor rhinitis, irregular size of the pupils and often irregular pupillary reactions, bronchial spasm, nervous dyspepsia, irregular heart beats, irregular urinations, defecations and sexual functioning, the cause for these departures from health is an imbalance of the autonomic nervous system.

Anatomy. The autonomic system consists in part of a series of nerve centers situated in the diencephalon, mainly in the hypothalamus, the floor of the third ventricle and the periaqueductal gray matter. In health these centers are influenced but not controlled by the cerebral cortex.

The autonomic nervous system has two great subdivisions—the *sympathetic system* or the thoracolumbar outflow, and the *parasympathetic* which includes the craniocervical and sacral outflows of nerves These autonomic subdivisions are not as separately distinct functionally as they are anatomically. The functional overlapping has been explained on the basis of chemical mediators utilized in the transmission of nerve impulses When choline is the dominant chemical mediator the nerves (parasympathetic) are designated cholinergic and when epinephrine is the dominant chemical mediator the nerves (sympathetic) are designated adrenergic nerves.

It may be of etiologic significance to observe that the impulses of both of these subdivisions of the autonomic system are mediated by hormones The sympathetics are mediated by the hormone epinephrine and the parasympathetics by the hormone acetylcholine of plant origin, a vitamin.

Sympathetic Division. The sympathetic division or thoracolumbar outflow of the autonomic system consists of a series of ganglia connected by a trunk of nerve fibers situated one on each side, and in front of the vertebral column, and extending from the atlas to the coccyx where they fuse in a ganglion

Each trunk consists of nerve cells which only give off involuntary efferent nerve fibers,

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variations. It is usually benign Neurofibroma (von Recklinghausen's disease) usually involves the peripheral nerves. However, the cranial nerves may be affected and particularly the vagi. These tumors are benign

The benign autonomic tumors are usually accidental, surgical or necropsy findings.

In most instances imbalance is of a mild degree and therefore goes unnoticed by the patient. In some, however, the imbalance is excessive and is the cause of complaint or of manifestations Imbalance of each division of the autonomic system will be discussed in its appropriate place.

Symptoms. Stimulation of the *sympathetic* nerves occurs in many normal reflex reactions of the body, for instance, during emotional states and severe pain Stimulation occurs in association with the mobilization of epinephrine and thus it is termed adrenergic reactions.

The signs of stimulation are best observed in the eye. These signs are often present in exophthalmic goiter (Graves's or Basedow's disease). Stimulation of these sympathetic nerves may be artificially induced by the administration of a few drops of a solution (5 to 10 per cent) of cocaine. Soon after administration of this drug there is a dilatation of the pupil, exophthalmos, proptosis, or forward projection of the eyeball; widening of the palpebral aperture (Dalrymple's sign); infrequency of involuntary blinking (Stellwag's sign); oculopalpebral asynergia, producing delayed descent of the upper lid when the patient looks downward, leaving a band of white sclerotic visible between the upper lid and the cornea (von Graefe's sign); and deficient convergence of the eyeballs (Möbius' sign).

Stimulation of the sympathetic nerves produces, in addition to the eye signs, tachycardia, sweating, dryness of the mucous membranes of the nose and mouth, dyspnea, hyperglycemia, atonic intestines, impotence and spermatorrhea.

In former years a congenital form of hyperactivity of the sympathetic nerves was recognized and described, and termed *sympathicotonia*. This congenital sympathicotonia was supposed to produce a definite somatic type.

It was thought that preponderance of sympathetic nerve activity was inheritable. Those inheriting sympathicotonia are adrenergic individuals who have very active (but still within normal limits) adrenal glands Such a person is lively and excitable, with rapid heart, bright eyes, mobile and dilated pupils, rosy color, deficient acidity of the gastric juice, and a warm, dry skin Sympathicotonic individuals are specially sensitive to epinephrine, to thyroid secretion and to posteropituitrin, any one of which exaggerates all their characteristics The oculocardiac and carotid-sinus reflexes are often diminished or absent

The important reflexes which the craniocervical outflow of *parasympathetic* fibers subserves are the pupillary reflex, the secretion of saliva and gastric juice, the maintenance of muscular tonus of the alimentary canal, the vagus control of insulin secretion, and the tonic vagal slowing of the heart rate

Parasympathetic stimulation is manifested by miosis, slowness and diminished force of the heart, contraction of the uterus, ureters, bladder, and bronchial muscle; contraction of the colon with relaxation of the internal rectal sphincter, paresis of the intra-abdominal blood vessels, lowered blood pressure, pallor of the skin, and increase of glandular secretions. There are lacrimation, nasal congestion, salivation, priapism, pollakiuria, gastric hyperacidity, and hypermobility and spasm of the pylorus and the esophagus

The parasympathetic fibers and end organs are specially stimulated by insulin.

Like the sympathetic subdivision with its congenital form of sympathicotonia an increased activity of the parasympathetic nerves causes a *parasympathicotonia* which is usually termed vagotonia.

Vagotonia may be a family characteristic. It may be generalized all through the body, or, more commonly, it is a localized vagotonia, limited to the cranial, the cervical, or the sacral division of the parasympathetic system.

The parasympathetic, cholinergic, or vagotonic type of individual, with low

to gland tissue, to blood vessels, and to organs which possess unstriated muscle fibers. Each cord or trunk is connected with the spinal cord by both white and gray rami communicantes

Parasympathetic Division. The parasympathetic division of the autonomic nerves has its cells of origin in special nuclei in the brain stem, in the midbrain and nucleus lateralis in the medulla, which are homologous with the intermediolateral nuclei in the spinal cord Through the vagus nerves fibers are distributed to the thorax and the abdomen The anteriorly situated autonomic nuclei are associated with the control of parasympathetic reflexes

The sacral outflow of parasympathetic fibers emerges from the spinal cord through the second, third, and fourth sacral nerves of the cauda equina The white rami are given off from the nerve roots after they have emerged through the sacral foramina The parasympathetic pelvic nerves (nervi erigentes) run directly into the hypogastric plexus in the hollow of the sacrum, and thence to the muscular walls of the colon, rectum, bladder and urethra and the genital organs, affording reflex paths for the emptying of these hollow organs in the presence of the continuous, tonic, or postural influence of the sympathetic nerves

The parasympathetic division is distributed to ganglia arranged in peripheral plexuses on the surface of the individual viscera supplied, for example, in the intestine, Auerbach's plexus between the two layers of the muscular coat, and Meissner's plexus in the submucosa

Autonomic Reflexes. The autonomic nervous system is concerned with two classes of reflexes In one, the centripetal path runs in a cerebrospinal nerve, and the stimulus, on reaching the brain stem, is reflected peripherally along a fiber of the autonomic system Examples of these reflexes are salivation, sweating, flushing of the skin and the genital reflex In the other class of autonomic reflex both afferent and efferent paths are outside of the brain stem. This reflex arc is contained in the peripheral plexuses and regulates the movements of hollow organs such as the gastrointestinal tract, uterus, ureters and bladder

Etiology of Autonomic Disorders. All disorders of the autonomic nervous system are caused by imbalances of activity between the two subdivisions irrespective of whether the subdivisional separation has been made on the bases of anatomy or physiology The functions of the divisions are, in health, synergistic. This synergism is maintained by (1) acid-base equilibria, (2) vasosensory mechanisms, (3) endocrine and exocrine secretions, (4) autonomic reflexes and (5) central controls.

Pathology of Autonomic Disorders. In most instances it is impossible to establish a direct anatomic or a histologic relationship between the neural lesions and the clinical manifestations of autonomic hypertonus or imbalance.

The changes described in the autonomic cells present in the aging patient are termed senile degeneration In acute or chronic disease in younger patients, chromidial alterations, pigment increases, changes in the pigments and their distribution within the cells, vacuoles in ganglion cells, neuronophagia, hyaline degeneration, hydropic alteration, shrinkage, neurofibrillar changes, modification of the dendrites and changes in the interstitial cells have been observed to be incident to many acute and chronic infections and vasospastic conditions

A common cause for lesions of the hypothalamus is infection, both bacterial and viral. As has been stated in various parts of this text hypothalamic disturbances are often associated with epidemic encephalitis. In instances of measles associated with encephalitis there are present perivascular demyelinization, glial proliferation, congestion and hemorrhage in the hypothalamus The less common causes for hypothalamic disorders are: scarlet fever, pertussis, diphtheria, mumps, typhoid fever and lymphocytic meningoencephalitis.

Imbalance of the autonomic nervous system may be due to tumors Tumors are commoner in the autonomic nervous system than in the central nervous system and also commoner in the parasympathetic division than in the sympathetic division of autonomic nerves Both benign and malignant tumors occur in both divisions

Benign tumors of autonomic nerves are ganglioneuroma, paraganglioma and neurofibroma The ganglioneuroma is usually benign but may become malignant if there are present groups of immature cells within the tumor The paraganglioma exhibits many

is due to the narrowed palpebral fissure, the drooping of the upper eyelid and to a distinct elevation of the lower lid. On palpating the two eyeballs the intra-ocular tension is observed to be diminished on the affected side.

When the cervical sympathetic is paralyzed, the ciliospinal reflex is abolished; pinching or pricking the side of the neck will not produce a dilatation of the pupil. A few minims of a 5 to 10 per cent solution of cocaine in the eye on the affected side will not cause the pupil to dilate, neither will the upper lid retract, nor will the eyeball be pushed slightly forward.

In an occasional instance of cervical sympathetic palsy, some degree of facial hemiatrophy may occur, but this is never so pronounced as in idiopathic facial hemiatrophy (see the Face, Chapter 4).

Horner's syndrome must be differentiated from Adie's syndrome, a condition not known to be due to any lesion of the central nervous system, characterized by a pathologic pupil reaction (pupillotonia) In Adie's syndrome there is a myotic condition on accommodation, the pupil on the affected side contracts on near vision more slowly than does the pupil on the opposite side, and it also dilates more slowly. The affected pupil does not react to direct or indirect light or it may do so in abnormal fashion

Skin, Mucous Membranes and Joints All autonomic skin disturbances except for those of the face are sympathetic in origin. The sympathetic paths arise in the brain stem and descend along extrapyramidal tracts of the spinal cord, to end in the lateral horns, where lower autonomic centers are situated, which affect circulatory, vasomotor and sudomotor activities

Sweating is produced by direct stimulation of the sympathetic reflex centers in the spinal cord, medulla, hypothalamus or cerebral cortex Sweating is increased by (1) rise of external or internal body temperature, (2) emotional states, (3) exercise, (4) nausea, vomiting, asphyxia, anoxia and often during normal sleep The quantity of sweat which can be produced in an hour is between 1,500 and 2,000 ml

Interruption of continuity of a cutaneous nerve produces an area of abnormal dryness corresponding to that of the sensory loss The skin becomes thin and glossy. The nails are hardened, become ridged and brittle, and grow more rapidly than normal nails Incomplete disruption of mixed nerve trunks, such as the median or sciatic, is associated with excessive sweating of the affected hand or foot Alopecia often follows lesions of the autonomic nerves

The hemiplegic state caused by lesions of the capsule is attended by excessive sweating of the hand, foot and axilla on the paralyzed side If the hemiplegia is due to a striatal lesion the face shares in the hemihyperidrosis

Transections of the spinal cord may be associated with abnormalities of sweating Above the level of the lesion, profuse sweating is induced, whereas the skin of the trunk and legs remains dry up to the level of the transection.

Localized symmetrical sweating of the palms and soles may be occasioned by mental exertion and emotional excitement. In the rest of the body the skin remains dry

The cutaneous [illegible]
nomenon, acrocya [illegible]
stimulation eviden [illegible]
ciation with the peripheral vascular diseases (Chapter 6).

Gustatory sweating affecting the face or other parts of the body (i e., the knee or knees) occurs in some otherwise normal persons; unilateral or bilateral redness and sweating of the face may occur when chewing substances of particular flavor. Other cases of unilateral flushing and sweating of the face occur after injury to the parotid gland on the same side, chiefly in the area of the auriculotemporal nerve.

Angioneurotic edema (Quincke's disease) depends on a vasomotor disturbance associated with the absorption of toxins, exogenous or endogenous, to which the

suprarenal activity, is reserved and "cold-blooded," with slow pulse, low blood pressure, contracted pupils, deep-set eyes, cool, pale skin which sweats easily and sometimes patchily; also clammy hands and feet. Vagotonic individuals often show other evidence of excessive vagal activity in the form of gastric hyperacidity, bradycardia, asthma, mild respiratory arrhythmia of the heart, and spastic constipation, analogous to the asthmatic bronchial spasm. Sugar tolerance is high, so that relatively large amounts of glucose can be taken without inducing glycosuria Also, the blood shows a tendency to eosinophilia.

The oculocardiac and carotid-sinus reflexes are especially active in vagotonic individuals

Vagotonic women sometimes have a masculine distribution of the pubic hair, which, instead of being bounded above by a horizontal line, extends upward along the linea alba toward the umbilicus. Such women have small mammary glands and often a ring of hair around the nipples.

The manifestations of parasympathetic paralysis are: decreased secretion of the skin of the face, mucous membranes of the mouth, nose, throat, eyes, respiratory passages, salivary glands, stomach and pancreas. All unstriped muscle except arterial walls seems to be affected when the inhibitory power of the vagus is removed.

EYE. In the eye sympathetic fibers innervate the radial or dilator fibers of the iris, the smooth muscle of the upper lid and the blood vessels of the eyeball. The pupil-dilating fibers arise from a cortical center in the frontal lobe, and descend by way of the hypothalamus and the brain stem into the lateral column of the spinal cord. They pass from the cord as preganglionic fibers through the anterior roots of the first and second thoracic segments, and to the inferior cervical ganglion by white rami communicantes They now ascend in the cervical sympathetics to the gasserian ganglion, and thence to the orbit along the ophthalmic division of the fifth cranial nerve, through the long ciliary nerves to the pupil.

The parasympathetic craniocervical outflow arises from laterally placed nuclei in the midbrain and passes with the oculomotor nerve to the ciliary ganglion and thence to the iris and ciliary muscle, or from the medulla passes along with the nervus intermedius, glossopharyngeal, and vagus nerves to the sphenopalatine, otic, and submaxillary ganglia The parasympathetic fibers innervate the constrictor muscle of the iris and ciliary muscle. The latter mediate the light reflex and accommodation

Horner's Syndrome. A unilateral lesion with paralysis of the cervical sympathetic nerves causes Horner's syndrome. This syndrome may be caused by a variety of lesions at different sites, for instance. (1) lesions of the brain stem; (2) intramedullary lesions of the spinal cord at or about the level of the first thoracic segment, (3) extramedullary lesions of the spinal cord; (4) lesions involving the peripheral portion of the cervical sympathetic

On examination in unilateral paralysis of the cervical sympathetic the eyelid on the side of the lesion droops and the affected side of the face flushes less than the normal side and there may be gustatory hyperhidrosis of the affected side of the face From paralysis of the dilator pupillae the affected pupil is smaller than the other. The affected pupil does not dilate when protected from the light; yet it contracts promptly to light and on convergence. Contraction and convergence of the pupil are affected by the sphincter pupillae which is innervated by the third cranial nerve through the ciliary ganglion The affected upper lid droops owing to paralysis of the unstriated (involuntary) part (tarsalis superior) of the levator palpebrae The voluntary, striated fibers of the levator, inserted into the skin of the upper lid and supplied by the oculomotor nerve, are unaffected, and the patient is therefore able to elevate the lid voluntarily to its full extent. The drooping of the affected upper lid therefore, is not a true ptosis, but a "pseudoptosis"

The affected eye seems to be sunk into the orbit This apparent enophthalmos

at irregular intervals. There is rarely a loss of consciousness. The attack is often alleviated by small doses of glyceryl trinitrate (see Chapter 5).

Vagotonia and Bronchial Asthma. The paroxysmal expiratory dyspnea of bronchial asthma, with its slow and labored breathing, is associated with excessive vagotonia. The phenomena, which in some cases constitute an allergic reaction, are produced by spasm of the unstriated bronchial muscles, innervated by parasympathetic fibers of the vagus. It is for this reason that many instances of asthma are found not to be of allergic origin

Abdomen and Pelvis In the section on Endocrine Disorders of the Pancreas (Chapter 14) under the heading Hypoglycemia are mentioned instances of hypoglycemia without other evidence of hyperinsulinism. In these patients there is no convulsive disorder associated with the hypoglycemia. This condition, in some, is thought to be due to an abnormal activity of the parasympathetic nerves to the pancreas.

Nervous Dyspepsias. Anxiety psychoneuroses are often associated with visceral symptoms and especially dyspepsia. In such cases, interference with the motor and secretory functions of the gastrointestinal tract may result from purely psychogenic causes, acting through the autonomic system.

Dyspepsias of nervous origin are often associated with hyperacidity and pyloric spasm, and excessively loud peristaltic rumbling noises. The rare condition known as acute dilatation of the stomach, and many of the symptoms of acute peritonitis, such as intestinal paralysis, meteorism, small pulse and general collapse, may be the result of acute paralysis of the parasympathetic fibers of the solar plexus Irritation of the solar plexus, and especially of its parasympathetic fibers, is exemplified in cases of lead colic, with its associated pain, constipation, and increased arterial tension The various visceral "crises" of tabes dorsalis—gastric, intestinal, renal and rectal—may be due to syphilitic changes in the autonomic fibers traversing the posterior spinal nerve roots, either irritative or causing defective inhibition. In sympathetic crises, pain is the main symptom which may be associated with cutaneous hyperesthesia of the abdominal wall.

Other digestive disorders associated with autonomic imbalance such as hypertrophic stenosis of the pylorus, spasm of the pylorus in adults giving symptoms resembling those of peptic ulcer, intussusception of the small intestine in children, chronic diarrhea and constipation and often indeterminate abdominal pains are described in Chapter 13.

The hypogastric plexus or presacral nerve, which supplies the pelvic viscera, receives its sympathetic fibers from the upper two lumbar ganglia and, after dividing into the two pelvic plexuses, one on each side of the rectum or vagina, receives sacral parasympathetic fibers through the second, third, and fourth sacral nerves, the combined strands constituting the nervus erigens on each side

The pelvic plexuses send nerve fibers to the terminal ganglia innervating the pelvic colon, rectum, bladder, uterus, fallopian tubes and internal genital organs

Many of the disorders which may arise in disturbances of the hypogastric plexus have been described with the diseases of the abdomen Among these disorders is hypertrophy and dilatation of the colon with constipation or Hirschsprung's disease (see Diseases of the Colon in Chapter 13).

There are syndromes manifested by pain (for instance, menstruation) associated with the normal physiologic functioning of the organs within the pelvis. Other syndromes are associated with a dissatisfaction with functioning of the distal colon, rectum and internal and external genitalia. These syndromes, many of them bizarre, are difficult to interpret. It is known, however, that the sympathetic nerves cause the uterus to contract, whereas the parasympathetic nerves inhibit contraction

Stimulation of the presacral nerve or the lumbar sympathetic fibers contracts the seminal vesicles, ejaculatory ducts and muscular septa of the prostate, which causes a pouring out of seminal fluid and prostatic secretion into the prostatic urethra. If

individual is hypersensitive. In those who have an allergic state by inheritance it may be associated with the intake of special articles of food. In some a crisis may occur which closely resembles anaphylactic attacks The attacks tend to recur for several months to years and then a long period, several years, may supervene without manifestations of the disorder.

When angioneurotic edema occurs in paroxysms the condition is known as Quincke's disease. Quincke's disease is characterized by paroxysmal attacks of sharply localized edema in various parts of the face, trunk, or limbs. After lasting a few hours, the swelling passes off spontaneously. The mucous membranes of the respiratory or gastrointestinal tract may be affected If the gastric mucous membrane is affected there is urgent vomiting, if the intestinal mucous membrane be affected a colic, and bloody diarrhea ensue, and if the mucous membrane of the larynx is severely affected death may result from edema of the glottis and asphyxia When the joints are affected, especially the knee joint, the condition is known as *intermittent hydrarthrosis*. The joint suddenly becomes distended with fluid, accompanied by a feeling of tightness and pain The swelling of the joint disappears in three or four days without residual disability to the joint and without fever though a leukocytosis may be present

Some varieties of urticaria are referable to affection of the vasomotor nervous mechanism, as in cases in which the characteristic itching wheals appear on sudden emotional excitement

In the hemiplegic state it is common to find edema of the hand or foot on the paralyzed side Permanent coldness and cyanosis are common in the paralyzed limbs of old poliomyelitics. Even in warm weather, the flaccid limb remains cold, and sometimes blue

The vasomotor fibers to the skin are not trophic fibers. The trophic nerve fibers seem to be closely associated with the vasomotor fibers and probably course with the latter to the skin Trophic disturbances follow aberrations in function of the autonomic nerves which may occur as sequelae of poliomyelitis, tabes dorsalis, and syringomyelia Disturbance of the functions of the urinary bladder is closely associated with trophic disturbances

HEART AND LUNGS. The sympathetic innervation of the heart is through the superior, middle and inferior cardiac nerves from the cervical ganglia similarly termed. There are additional innervations through rami from the sympathetic trunk in the thorax The efferent components are postganglionic fibers from the sympathetic ganglia The parasympathetic innervation is through three rami of the vagus nerve. The efferent components are preganglionic fibers from the cardiac plexuses

The proximal portions of the aorta, pulmonary artery and the cardiac wall, the cardio-aortic zones, are supplied in addition to the sympathetic fibers, by depressor nerves from the vagus Both afferent and efferent sensory cerebrospinal nerves are present in the cardio-aortic zones

Vasovagal Attacks. The paroxysms termed vasovagal attacks appear to be due to disorder of that part of the hypothalamic region which concerns the vagal distribution to the heart, lungs, and other viscera. The disorder is more frequent in women at the menopause and in younger women with pelvic disorders than in other persons

The attack generally begins with an epigastric aura, quickly followed in some instances by violent, irregular and rapid beating of the heart (*transient auricular* [illegible] constriction, *suffocative* dyspnea and [illegible] ases after the onset of the attack [illegible] ace is pale, and the limbs become cold. The pulse rate may fall to 30 per minute or less. This is followed either by burning flushes or clammy sweat, and by a tension of the muscles, sometimes amounting to tetany.

The paroxysms vary in duration from a few minutes to several hours and recur

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the lumbar sympathetics are bilaterally divided for the relief of congenital megacolon or of some angiospastic disorder in the lower limbs, the power of seminal ejaculation is lost, although in other respects the sexual reflex is unimpaired.

The sympathetic innervation retards the detrusor muscle of the bladder and excites the sphincter, while the parasympathetic innervation excites the detrusor muscle and inhibits the sphincter.

Examination. All through this book mention has been made in regard to the examination and significance of partial ptosis of the upper lids of the eyes, enophthalmos and miosis of the pupil. Dilatation of the pupil has many causes and not all dilatations are of autonomic origin

Aberrations of sweating over patches of the skin or in localized areas are always due to disturbances of the sympathetic nerves

A convenient method of mapping out sweating from nonsweating areas, according to Wright, is to paint the skin with a solution (the number of parts of some ingredients has been modified here) containing 1.5 gm. of pure iodine, 10 ml of oleum ricini and a sufficient quantity of alcohol (80 per cent) to make 100 ml After this has evaporated, leaving a thin film of oil and iodine, the skin is sprinkled with rice powder, and the powder is rubbed in; the excess is blown off with a fan. The patient is then exposed to a warm temperature Any sweating area will now appear as a deep blue-black color, the nonsweating areas remaining unchanged Another method of testing for abnormalities in sweating more convenient to the physician but uncomfortable to the patient is application of mustard to the patient's tongue which causes vasodilatation and sweating

The vasomotor reactions of the extremities to hot and cold water are described in association with diseases of the peripheral vascular system of the extremities (see Chapter 6)

A simple and practical method of examination of the skin of the extremities is to search for signs of cyanosis, pallor and scleroderma. Dermatographia is a sign of disordered vasomotor tone. Roughened, thickened, colorless nails, and other trophic changes may be present

By means of special thermometers differences in skin temperatures over localized areas or over extremities may be compared. This procedure is of great value in the diagnosis of the angioneuroses

Locally bony and soft tissue hypertrophy, Charcot joints with their increased mobility, are significant of autonomic disorders which accompany tabes dorsalis, syringomyelia, injuries and tumors.

In the syndrome of acroparesthesia there is present vasomotor disturbance of pale cold hands, paresthesias all of which may be an early stage of the cold wet cyanotic fingers and hands of Raynaud's phenomenon

The methods of examinations in the syndromes referable to the great autonomic plexuses are those commonly used for the detection of all manner of disease affecting the organs of the thorax, abdomen and pelvis

Diagnosis. The imbalances of the autonomic nervous system vary greatly in their clinical importance. These imbalances vary from manifestations which are accompanied by no ill health to those which are present in grave illnesses Since the autonomic nervous system is concerned with homeostasis no manifestation of imbalance can be taken lightly until it has been fully evaluated

In the diagnosis of autonomic disease it will be observed that sympathetic imbalances are more likely to be constant under any given conditions whereas parasympathetic imbalances are phasic and usually of short duration.

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